Genome-wide associations for birth weight and correlations with adult disease

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Birth weight (BW) is influenced by both foetal and maternal factors and in observational studies is reproducibly associated with future risk of adult metabolic diseases including type 2 diabetes (T2D) and cardiovascular disease[1]. These lifecourse associations have often been attributed to the impact of an adverse early life environment. We performed a multi-ancestry genome-wide association study (GWAS) meta-analysis of BW in 153,781 individuals, identifying 60 loci where foetal genotype was associated with BW ($P<5x10^{-8}$). Overall, ~15% of variance in BW could be captured by assays of foetal genetic variation. Using genetic association alone, we found strong inverse genetic correlations between BW and systolic blood pressure ($r_g=-0.22$, $P=5.5x10^{-13}$), T2D ($r_g=-0.27$, $P=1.1x10^{-6}$) and coronary artery disease ($r_g=-0.30$, $P=6.5x10^{-9}$) and, in large cohort data sets, demonstrated that genetic factors were the major contributor to the negative covariance between BW and future cardiometabolic risk. Pathway analyses indicated that the protein products of genes within BW-associated regions were enriched for diverse processes including insulin signalling, glucose homeostasis, glycogen biosynthesis and chromatin remodelling. There was also enrichment of associations with BW in known imprinted regions ($P=1.9x10^{-4}$). We have demonstrated that lifecourse associations between early growth phenotypes and adult cardiometabolic disease are in part the result of shared genetic effects and have highlighted some of the pathways through which these causal genetic effects are mediated.

We combined GWAS data for BW in 153,781 individuals representing multiple ancestries from 37 studies across three components (**Extended Data Fig. 1 and Supplementary Table 1**): (i) 75,891 individuals of European ancestry from 30 studies; (ii) 67,786 individuals of European ancestry from the UK Biobank; and (iii) 10,104 individuals of diverse ancestries (African American, Chinese, Filipino, Surinamese, Turkish and Moroccan) from six studies. Within each study, BW was z-score transformed separately in males and females after excluding non-singletons and premature births and adjusting for gestational age where available. Genotypes were imputed using reference panels from the 1000 Genomes (1000G)[2] or combined 1000G and UK10K Project[3] (**Supplementary Table 2**). We performed quality control assessments to confirm that the distribution of BW was consistent across studies, irrespective of the data collection protocol, and confirmed that self-reported BW in UK Biobank showed genetic and phenotypic associations consistent with those seen for measured BW in other studies[4] (**Methods**).

We identified 60 loci (59 autosomal) associated with BW at genome-wide significance ($P<5x10^{-8}$) in either the European ancestry or trans-ancestry meta-analyses (**Extended Data Fig. 2a, Extended Data Table 1a and Supplementary Data; Methods**). At lead SNPs, we observed no heterogeneity in allelic effects between the three study components (Cochran's *Q* statistic $P>0.00083$) (**Supplementary Table 3**). Fifty-three of these loci were novel in that the lead SNP mapped >2Mb away from, and was statistically independent (EUR $r^2<0.05$) of, the seven previously-reported BW signals[5], all of which were confirmed in this larger analysis (**Supplementary Table 4**). Approximate conditional analysis in the European ancestry data indicated that three of these novel loci (near *ZBTB7B, HMGA1* and *PTCH1*) harboured multiple distinct association signals attaining genome-wide significance (**Methods**; **Supplementary Table 5 and Extended Data Fig. 3**).

The lead variants for most signals mapped to non-coding sequence, and at only two loci, *ADRB1* (rs7076938; $r^2=0.99$ with *ADRB1* G389R) and *NRIP1* (rs2229742, R448G) did the association data point to likely causal non-synonymous coding variants (**Supplementary Table 6; Methods**). Lead SNPs for all but two loci (those mapping near *YKT6-GCK* and *SUZ12P1-CRLF3*) were common (minor allele frequency (MAF) ≥5%) with individually modest effects on BW (β=0.020-0.053 standard deviations (SD) per allele, equivalent to 10-26g). This was despite much improved coverage of low-frequency variants in this study (compared to previous HapMap 2 imputed meta-analyses[5]) reflecting imputation from larger, and more complete, reference panels (**Extended Data Table 1b**). Indeed, all but five of the common variant association signals were tagged by variants (EUR $r^2>0.6$) in

the HapMap 2 reference panel (**Supplementary Tables 4, 5**), indicating that most of the novel discovery in the present study was driven by increased sample size[5]. Fine-mapping analysis yielded 14 regions within which fewer than ten variants contributed to the locus-specific credible set that accounted for >99% of the posterior probability of association (**Methods; Supplementary Table 7**). The greatest refinement was at *YKT6-GCK*, where the credible set included only the low frequency variant rs138715366, which maps intronic to *YKT6.* These credible set variants collectively showed enrichment for overlap with DNaseI hypersensitivity sites, particularly those generated, by ENCODE, from foetal (4.2-fold, 95% CI [1.8-10.7]) and neonatal tissues (4.9 [1.8-11.0]) (**Supplementary Fig. 1 and Supplementary Table 8; Methods**).

In combination, the 62 distinct genome-wide significant signals at the 59 autosomal loci explained 2.0% (standard error (SE) 1.1%) of variance in BW (**Supplementary Table 9; Methods**), similar in magnitude to that attributable to sex or maternal body mass index (BMI)[5]. However, the variance in BW captured collectively by all autosomal genotyped variants on the array was considerably larger, estimated at 15.1% (SE=0.9) in UK Biobank (**Methods**). These figures are consistent with a long tail of genetic variants of smaller effects contributing to variation in BW.

Associations between foetal genotype and BW could result from indirect effects of the maternal genotype influencing BW via the intrauterine environment given the correlation ($r \approx 0.5$) between maternal and foetal genotype. However, two lines of evidence indicated that variation in the foetal genome was the predominant driver of the BW associations. First, an analysis of the global contribution of maternal vs. foetal genetic variation, using a maternal-GCTA model[6] (**Methods**) applied to 4,382 mother-child pairs, estimated that the child's genotype (σ_C^2=0.24, SE=0.11) makes a larger contribution to BW variance than either the mother's genotype (σ_M^2=0.04, SE=0.10), or the covariance between the two (σ_{CM}=0.04, SE=0.08). Second, when we compared the point estimates of the BW effect size dependent on maternal genotype at each of the 60 loci (as measured in up to 68,254 women[7]) with those dependent on foetal genotype (using European ancestry data from 143,677 individuals in the present study), foetal variation had greater impact than maternal at 93% of loci (55/60; binomial P=1x10^{-11}) (**Supplementary Table 10, Extended Data Figs 4, 5**; **Methods**). Power to further disentangle maternal and foetal contributions using analyses of foetal genotype conditional on maternal genotype was constrained by the limited sample size available (n=12,909 mother-child pairs) (**Supplementary Table 11**).

Collectively, these analyses provide compelling evidence that foetal genotype has a substantial impact on early growth, as measured by BW. We sought to use these genetic associations to understand the causal relationships underlying observed associations between BW and disease, and to characterise the processes responsible.

To quantify the shared genetic contribution to BW and other health-related traits, we estimated their genetic correlations using LD Score regression[8] (**Methods**). BW (in European ancestry samples) showed strong positive genetic correlations with anthropometric and obesity-related traits including birth length (r_g=0.81, P=2.0x10^{-44}), and in adults, height (r_g=0.41, P=4.8x10^{-52}), waist circumference (r_g=0.18, P=3.9x10^{-10}) and BMI (r_g=0.11, P=7.3x10^{-6}). In contrast, BW showed inverse genetic correlations with indicators of adverse metabolic and cardiovascular health including coronary artery disease (CAD, r_g=-0.30, P=6.5x10^{-9}), systolic blood pressure (SBP, r_g=-0.22, P=5.5x10^{-13}) and T2D (r_g=-0.27, P=1.1x10^{-6}) (**Fig. 1, Supplementary Table 12 and Supplementary Fig. 2**). These correlations between BW and adult cardiometabolic phenotypes are of similar magnitude, although directionally-opposite, to the reported genetic correlations between adult BMI and those same cardiometabolic outcomes[8]. These findings support observational associations between a history of paternal T2D and lower BW[4], and establish more generally that the observed lifecourse associations between early growth and adult disease, at least in part, reflect the impact of shared genetic variants that influence

both sets of phenotypes. In an effort to estimate the extent of genetic contribution to these lifecourse associations, we first focused on data from UK Biobank (n=57,715). For many of the traits for which data were available, genetic variation contributed substantially to the lifecourse relationship between BW and adult phenotypes, and in some cases appeared to be the major source of covariance between the traits. For example, we estimated that 85% (95% CI=70%-99%) of the negative covariance between BW and SBP was explained by shared genetic associations captured by directly genotyped SNPs (**Supplementary Table 13; Methods**). For continuous cardiometabolic measures, including lipids and fasting glycaemia, for which measures are not currently available in UK Biobank, we turned to the Northern Finland Birth Cohort (n=5,009), and obtained similar results (**Supplementary Table 13**). However, these estimates are limited, not only by wide confidence intervals, but also by the assumption of a linear relationship between BW and each of the phenotypes and by the inability to explicitly model maternal genotypic effects. In other words, the inverse genetic correlations between BW and cardiometabolic traits may not exclusively reflect genetic effects mediated directly through the offspring, but also effects mediated by maternal genotype acting indirectly via perturbation of the *in utero* environment. Nevertheless, these estimates indicate that a substantial proportion of the variance in cardiometabolic risk that covaries with BW can be attributed to the effects of common genetic variation.

To elucidate the biological pathways and processes underlying regulation of foetal growth, we first performed gene set enrichment analysis of our BW GWAS analysis using MAGENTA[9] (**Methods**). Twelve pathways reached study-wide significance (FDR<0.05), including pathways involved in metabolism (insulin signalling, glycogen biosynthesis, cholesterol biosynthesis), growth (IGF-signalling, growth hormone pathway) and development (chromatin remodelling) (**Extended Data Table 2a**). Similar pathways were detected in a complementary analysis where we interrogated empirical protein-protein interaction (PPI) data identifying 13 PPI network modules with marked (z-score >5) enrichment for BW-association scores (**Extended Data Table 2b and Extended Data Figs 6a, b**; **Methods**). The proteins within these modules were themselves enriched for diverse processes related to metabolism, growth and development (**Extended Data Figs 6a, b**).

We also observed enrichment of BW association signals across the set of 77 imprinted genes defined by the Genotype-Tissue Expression (GTEx) project[10] (P=1.9x10^{-4}; **Extended Data Table 2a and Supplementary Table 14**). Such enrichment is consistent with the "parental conflict" hypothesis regarding the allocation of maternal resources to the foetus[11]. Although the role of imprinted genes in foetal growth is described in animal models and rare human disorders[12], our result is the first large-scale, systematic demonstration of their contribution to normal variation in BW. Of the 60 genome-wide significant loci, two (*INS-IGF2*, *RB1*) fall within (or near) imprinted regions (**Extended Data Fig. 2b**), with a noteworthy third signal at *DLK1* (previously foetal antigen-1; P=5.6x10^{-8}). Parent-of-origin specific analyses to further investigate these individual loci (comparing heterozygote vs. homozygote BW variance in 57,715 unrelated individuals, and testing BW associations with paternal vs. maternal alleles in 4,908 mother-child pairs; see **Methods**) proved, despite these sample sizes, to be underpowered (**Extended Data Fig. 7 and Supplementary Tables 15, 16**).

Many of the genome-wide signals for BW detected here are also established genome-wide association signals for a wide variety of cardiometabolic traits (**Fig. 2**). These include the BW signals near *CDKAL1, ADCY5, HHEX/IDE* and *ANK1* (also genome-wide significant for T2D), *NT5C2* (for blood pressure (BP), CAD and BMI) and *ADRB1* (for BP). We used two approaches to understand whether this pattern of adult trait association represented a generic property of BW-associated loci, or reflected heterogeneous mechanisms linking BW to adult disease.

First, we applied unsupervised hierarchical clustering (**Methods**) to the non-BW trait association statistics for the 60 significant BW loci**.** The resultant heatmap indicates the heterogeneity of locus-specific effect sizes across the range of adult traits (**Fig. 2 and Supplementary Table 17**). For example, it shows that the associations between BW-raising alleles and increased adult height are concentrated amongst a subset of loci including *HHIP* and *GNA12*, and highlights particularly strong associations with lipid traits for variants at the *TRIB1* and *MAFB* loci.

Second, we constructed trait-specific "point-of-contact" (PoC) PPI networks from proteins represented in both the global BW PPI network and equivalent PPI networks generated for each of the adult traits (**Methods; Extended Data Figs 6c-e**). We reasoned that these PoC PPI networks would be enriched for the specific proteins mediating the observed links between BW and adult traits, generating hypotheses that are amenable to subsequent empirical validation. To highlight processes implicated in specific BW-trait associations, we overlaid these PoC PPI with the 50 pathways over-represented in the global BW PPI network. These analyses revealed, for example, that proteins in the Wnt canonical signalling pathway were only detected in the PoC PPI network for BP traits. We can use these PPI overlaps to highlight the specific transcripts within BW GWAS loci that are likely to mediate the mechanistic links. For example, the overlap between the Wnt signalling pathway and the PoC PPI network for the intersection of BW and BP-related traits implicates *FZD9* as the likely effector gene at the *MLXIPL* BW locus (**Extended Data Fig. 6d and Supplementary Table 6**).

We focused our more detailed investigation of the mechanistic links between early growth and adult traits on two phenotypic areas: arterial BP and T2D/glycaemia. Across both the overall GWAS and specifically among the 60 significant BW loci, most BW-raising alleles were associated with reduced BP (**Figs 1, 2**): the strongest inverse associations were seen for the loci near *NT5C2, FES, NRIP1, EBF1* and *PTH1R.* However, we also observed locus-specific heterogeneity in the genetic relationships between BP and BW: the SBP-raising allele at *ADRB1*[13] is associated with higher, rather than lower, BW (**Extended Data Fig. 8a**). When we considered the reciprocal relationship, i.e. the effects on BW of BP-raising alleles at 30 reported loci for SBP[13,14], there was an excess of associations (5/30 with lower BW at $P<0.05$; $P=0.0026$; **Extended Data Fig. 8a**). To dissect maternal and foetal genotype effects at these loci, we tested the impact on BW of a risk score generated from the 30 SBP SNPs, restricted to the untransmitted maternal haplotype score[15] in a set of 5,201 mother-child pairs. Analysis of these loci indicated that maternal genotype effects on the intrauterine environment are likely to contribute to the inverse genetic correlation between SBP and BW (**Methods; Supplementary Table 18**), and was consistent with the results of a wider study of >30,000 women which demonstrated associations between a maternal genetic score for SBP (conditional on foetal genotype) and lower offspring BW[16].

The BP-raising allele with the largest BW-lowering effect maps to the *NT5C2* locus (index variant for BW, rs74233809, $r^2=0.98$ with index variant for BP, rs11191548[14]) and is also associated with lower adult BMI ($r^2=0.99$ with rs11191560[17]). The BW-lowering allele at rs74233809 is a proxy for a recently-described functional variant in the nearby *CYP17A1* gene ($r^2=0.92$ with rs138009835)[18]. The *CYP17A1* gene encodes the cytochrome P450c17α enzyme, CYP17[19], which catalyses key steps in steroidogenesis that determine the balance between mineralocorticoid, glucocorticoid and androgen synthesis. This variant is known to alter transcriptional efficiency *in vitro* and is associated with higher urinary tetrahydroaldosterone excretion[18]. *CYP17A1* is expressed in foetal adrenal glands and testes from early gestation[20] as well as in the placenta[21]. These data implicate variation in *CYP17A1* expression as a contributor to the observational association between low BW and adult hypertension[22].

When we examined 45 loci associated with CAD[23], the inverse genetic correlation between CAD and BW was concentrated amongst the five CAD loci with primary BP associations. This suggests that

genetic determinants of BP play a leading role in mediating the lifecourse associations between BW and CAD (**Extended Data Figs 8b, e**).

LD score regression analyses demonstrated overall inverse genetic correlation between lower BW and elevated risk of T2D (**Fig. 1**)**.** However**,** the locus specific heatmap indicates a heterogeneous pattern across individual loci (**Fig. 2**). To explore this further, we tested the 84 reported T2D loci[24] for association with BW. Some T2D risk alleles (such as at *ADCY5*, *CDKAL1* and *HHEX-IDE*) were strongly associated with lower BW, whilst others (e.g. *ANK1* and *MTNR1B*) were associated with higher BW (**Extended Data Fig. 8c**). This was in contrast with the BW effects of 422 known height loci[25] (**Extended Data Fig. 8d**), which showed a strong positive correlation consistent with the overall genetic correlation between height and BW, indicating that the growth effects of many height loci start prenatally and persist into adulthood.

The contrasting associations of T2D risk-alleles with both higher and lower BW are likely to reflect the differential impacts across loci of variation in the maternal and foetal genomes. Observational data link paternal diabetes with lower offspring BW[4] indicating that the inheritance of T2D risk alleles by the foetus tends, in line with the LD score regression analysis, to reduce growth. These relationships are consistent with the precepts of the "foetal insulin hypothesis"[26] and reflect the potential for reduced insulin secretion and/or signalling to lead to both reduced foetal growth and, many decades later, enhanced predisposition to T2D. In line with this, the inferred paternal transmitted haplotype score generated from the 84 T2D risk variants was associated with lower BW (P=0.045) in 5,201 mother-child pairs (**Methods**; **Supplementary Table 18**). In contrast, maternal diabetes is observationally associated with higher offspring BW[4], reflecting the impact of maternal hyperglycaemia to stimulate foetal insulin secretion. The contribution of genotype-dependent maternal hyperglycaemia to BW is in line with the evidence, from a recent study, that maternal genotype scores for fasting glucose and T2D (conditional on foetal genotype) were causally associated with higher offspring BW[16]. It is also consistent with the observation that a subset of glucose-raising alleles is associated with higher BW[7]. For example, the T2D-risk variant at *MTNR1B* (which also has a particularly marked effect on fasting glucose levels in non-diabetic indivudals[27,28]) was amongst the subset of BW loci (5/60) for which the BW effect attributable to maternal genotype exceeded that associated with the foetal genotype (maternal: β=0.048, P=5.1x10^{-15}; foetal: β=0.023, P=2.9x10^{-8}) (**Supplementary Table 10, Extended Data Figs 4, 5**). Thus, both maternal and foetal genetic effects connect BW to later T2D risk, albeit acting in opposing directions. When we categorised T2D loci using a classification of physiological function derived from their effects on related glycaemic and anthropometric traits[27], we found that T2D-risk alleles associated with lower BW were those typically characterised by reduced insulin processing and secretion without detectable changes in fasting glucose (the "Beta Cell" cluster in **Extended Data Fig. 8f**).

The *YTK6* signal at rs138715366 is notable, not only because the genetic data indicates that a single low-frequency non-coding variant is driving the association signal (see above) but because of the proximity of this signal to *GCK*. Rare coding variants in glucokinase are causal for a form of monogenic hyperglycaemia and lead to large reductions in BW when parental alleles are passed to their offspring[29]. In addition, common non-coding variants nearby are implicated in T2D-risk and fasting hyperglycaemia[28]. However, the latter variants are conditionally independent of rs138715366 (**Supplementary Table 19**) and show no comparable association with lower BW. Either rs138715366 acts through effector transcripts other than *GCK*, or the impact of the low-frequency SNP near *YKT6* on *GCK* expression involves tissue- and/or temporal-specific variation in regulatory impact.

In conclusion, we have identified 60 genetic loci associated with BW and used these to gain insights into the aetiology of foetal growth and into well-established, but until now poorly understood, lifecourse disease associations. The evidence that the relationship between early growth and later

metabolic disease has an appreciable genetic component contrasts with, but is not necessarily incompatible with, the emphasis on adverse early environmental events highlighted by the Foetal Origins Hypothesis[1]. As we have shown, these genetic effects reflect variation in both the foetal and the maternal genome: the impact of the latter on the offspring's predisposition to adult disease could be mediated, at least in part, through perturbation of the antenatal and early life environment. Future mechanistic and genetic studies should support reconciliation between these alternative, but complementary, explanations for the far-reaching lifecourse associations that exist between events in early life and predisposition to cardiometabolic disease several decades later.

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348 **FIGURE LEGENDS**
349
350 **Figure 1 | Genome-wide genetic correlation between birth weight and a range of traits and**
351 **diseases in later life.** Genetic correlation (r_g) and corresponding standard error between BW and the
352 traits displayed on the *x* axis are estimated using LD Score regression[8]. The genetic correlation
353 estimates (r_g) are colour coded according to their intensity and direction (red for positive and blue
354 for inverse correlation). WHRadjBMI=waist-hip ratio adjusted for body mass index, HOMA-
355 B/IR=homeostatic model assessment of beta-cell function/insulin resistance, HbA1c=Hemoglobin
356 A1c, BMD=bone mineral density, ADHD=attention deficit hyperactivity disorder. See Supplementary
357 Table 12 for references for each of the traits and diseases displayed.
358
359 **Figure 2 | Hierarchical clustering of birth weight loci based on similarity of overlap with adult**
360 **diseases, metabolic and anthropometric traits.** For the lead SNP at each BW locus (*x*-axis), z-scores
361 (aligned to BW-raising allele) were obtained from publicly available GWAS for various traits (*y*-axis;
362 see Supplementary Table 17). A positive z-score (red) indicates a positive association between the
363 BW-raising allele and the outcome trait, while a negative z-score (blue) indicates an inverse
364 association. BW loci and traits are clustered according to the Euclidean distance amongst z-scores
365 (see Methods). Squares are outlined with a solid black line if the BW locus is significantly ($P<5x10^{-8}$)
366 associated with the trait in publicly available GWAS, or with a dashed line if reported significant
367 elsewhere. WHRadjBMI=waist-hip ratio adjusted for body mass index.
368

METHODS

Ethics statement. All human research was approved by the relevant institutional review boards and conducted according to the Declaration of Helsinki. All participants provided written informed consent. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees.

Study-level analyses. Within each study, BW was collected from a variety of sources, including measurements at birth by medical practitioners, obstetric records, medical registers, interviews with the mother and self-report as adults (**Supplementary Table 1**). BW was *z*-score transformed, separately in males and females. Individuals with extreme BW (>5 SD from the sex-specific study mean), monozygotic or polyzygotic siblings, or preterm births (gestational age <37 weeks, where this information was available) were excluded from downstream association analyses (**Supplementary Table 1**).

Within each study, stringent quality control of the GWAS genotype scaffold was undertaken, prior to imputation (**Supplementary Table 2**). Each scaffold was then pre-phased and imputed[30,31] up to reference panels from the 1000G[2] or 1000G and UK10K Project[3] (**Supplementary Table 2**). Association of BW with each variant passing established GWAS quality control filters[32] was tested in a linear regression framework, under an additive model for the allelic effect, after adjustment for study-specific covariates, including gestational age, where available (**Supplementary Table 2**). Where necessary, population structure was accounted for by adjustment for axes of genetic variation from principal components analysis[33] and subsequent genomic control correction[34], or inclusion of a genetic relationship matrix in a mixed model[35] (**Supplementary Table 2**). We calculated the genomic control inflation factor (λ) in each study to confirm that study-level population structure was accounted for prior to meta-analysis.

Preparation, quality control and genetic analysis in UK Biobank samples. UK Biobank phenotype data were available for 502,655 participants[36]. All participants in the UK Biobank were asked to recall their BW, of which 279,971 did so at either the baseline or follow-up assessment visit. Of these, 7,686 participants reported being part of multiple births and were excluded from downstream analyses. Ancestry checks, based on self-reported ancestry, resulted in the exclusion of 8,998 additional participants reported not to be white European. Of those individuals reporting BW at baseline and follow-up assessments, 393 were excluded because the two reported values differed by more than 0.5 kg. For those reporting different values (≤0.5 kg) between baseline and follow-up, we took the baseline measure forward for downstream analyses. We then excluded 36,716 individuals reporting values <2.5 kg or >4.5 kg as implausible for live term births before 1970. In total 226,178 participants had data relating to BW that matched these inclusion criteria.

Genotype data from the May 2015 release were available for a subset of 152,249 participants from UK Biobank. In addition to the quality control metrics performed centrally by UK Biobank, we defined a subset of "white European" ancestry samples using a K-means (K=4) clustering approach based on the first four genetically determined principal components. A maximum of 67,786 individuals (40,425 females and 27,361 males) with genotype and valid BW measures were available for downstream analyses. We tested for association with BW, assuming an additive allelic effect, in a linear mixed model implemented in BOLT-LMM[37] to account for cryptic population structure and relatedness. Genotyping array was included as a binary covariate in all models. Total chip heritability (i.e. the variance explained by all autosomal polymorphic genotyped SNPs passing quality control) was calculated using Restricted Maximum Likelihood (REML) implemented in BOLT-LMM[37]. We additionally analysed the association between BW and directly genotyped SNPs on the X chromosome: for this analysis, we used 57,715 unrelated individuals with BW available and identified by UK Biobank as white British. We excluded SNPs with evidence of deviation from Hardy-Weinberg Equilibrium ($P<1\times10^{-6}$), MAF<0.01 or overall missing rate >0.015,

resulting in 19,423 SNPs for analysis in Plink v1.07 (http://pngu.mgh.harvard.edu/purcell/plink/)[38], with the first five ancestry principal components as covariates.

In both the full UK Biobank sample and our refined sample, we observed that BW was associated with sex, year of birth and maternal smoking (P<0.0015, all in the expected directions), confirming more comprehensive previous validation of self-reported BW[4]. We additionally verified that BW associations with lead SNPs at seven established loci[5] based on self-report in UK Biobank were consistent with those previously published.

European ancestry meta-analysis. The European ancestry meta-analysis consisted of two components: (i) 75,891 individuals from 30 GWAS from Europe, USA and Australia; and (ii) 67,786 individuals of white European origin from UK Biobank. In the first component, we combined sex-specific BW association summary statistics across studies in a fixed-effects meta-analysis, implemented in GWAMA[39] and applied a second round of genomic control[34] (λ_{GC}= 1.001). Subsequently, we combined association summary statistics from this component with UK Biobank in a European ancestry fixed-effects meta-analysis, implemented in GWAMA[39]. Variants failing GWAS quality control filters in UK Biobank, reported in less than 50% of the total sample size in the first component, or with MAF<0.1%, were excluded from the European ancestry meta-analysis. We aggregated X-Chromosome association summary statistics from UK Biobank (19,423 SNPs) with corresponding statistics from the European GWAS component using fixed effects *P*-value based meta-analysis in METAL[40] (max N=99,152).

We were concerned that self-reported BW as adults in UK Biobank would not be comparable with that obtained from more stringent collection methods used in other European ancestry GWAS. In addition, UK Biobank lacked information on gestational age for adjustment, which could have an impact on difference in strength of association compared to the results obtained from other European ancestry GWAS. However, we observed no evidence of heterogeneity in BW allelic effects at lead SNPs between the two components of European ancestry meta-analysis, using Cochran's Q statistic[41], implemented in GWAMA[39], after Bonferroni correction (P>0.00083) (**Supplementary Table 3**). We tested for heterogeneity in allelic effects between studies within the European component using Cochran's *Q*. At loci demonstrating evidence of heterogeneity, we confirmed that association signals were not being driven by outlying studies by visual inspection of forest plots. We performed sensitivity analyses to assess the impact of covariate adjustment (gestational age and population structure) on heterogeneity.

We were also concerned that overlap of individuals (duplicated or related) between the two components of the European ancestry meta-analysis might lead to false positive association signals. We performed bivariate LD Score regression[8] using the two components of the European ancestry meta-analysis and observed a genetic covariance intercept of 0.0156 (SE 0.0058), indicating a maximum of 1,119 duplicate individuals. Univariate LD Score regression[8] of the European ancestry meta-analysis estimated the intercept as 1.0426, which may indicate population structure or relatedness that is not adequately accounted for in the analysis. To assess the impact of this inflation on the European ancestry meta-analysis, we expanded the standard errors of BW allelic effect size estimates and re-calculated association *P*-values. On the basis of this adjusted analysis, the lead SNP only at *MTNR1B* dropped below genome-wide significance (rs10830963, P=5.5x10^{-8}).

Trans-ancestry meta-analysis. The trans-ancestry meta-analysis combined the two European ancestry components with an additional 10,104 individuals from six GWAS from diverse ancestry groups: African American, Chinese, Filipino, Surinamese, Turkish and Moroccan. Within each GWAS, we first combined sex-specific BW association summary statistics in a fixed-effects meta-analysis, implemented in GWAMA[39] and applied a second round of genomic control[34]. Subsequently, we combined association summary statistics from the six non-European GWAS and the two European ancestry components in a trans-ancestry fixed-effects meta-analysis, implemented in GWAMA[39]. Variants failing GWAS quality control filters in UK Biobank, reported in less than 50% of the total

sample size in the first component, or with MAF<0.1%, were excluded from the trans-ancestry meta-analysis. We tested for heterogeneity in allelic effects between ancestries using Cochran's Q[41].

Approximate conditional analysis. We searched for multiple distinct BW association signals in each of the established and novel loci, defined as 1Mb up- and down-stream of the lead SNP from the trans-ancestry meta-analysis, through approximate conditional analysis. We applied GCTA[42] to identify "index SNPs" for distinct association signals attaining genome-wide significance ($P<5x10^{-8}$) in the European ancestry meta-analysis using a reference sample of 5,000 individuals of white British origin, randomly selected from UK Biobank, to approximate patterns of linkage disequilibrium (LD) between variants in these regions. Note that we performed approximate conditioning on the basis of only the European ancestry meta-analysis because GCTA cannot accommodate LD variation between diverse populations.

Prioritising candidate genes in each BW locus. We combined a number of approaches to prioritise the most likely candidate gene(s) in each BW locus. Expression quantitative trait loci (eQTLs) were obtained from the Genotype Tissue Expression (GTEx) Project[43], the GEUVADIS Project[44] and eleven other studies[45-55] using HaploReg v4[56]. We interrogated coding variants for each BW lead SNP and its proxies (EUR $r^2>0.8$) using Ensembl[57] and HaploReg. Their likely functional consequences were predicted by SIFT[58] and PolyPhen2[59]. Biological candidacy was assessed by presence in significantly enriched gene set pathways from MAGENTA analyses (see below for details). We extracted all genes within 300 kb of all lead BW SNPs and searched for connectivity between any genes using STRING[60]. If two or more genes between two separate BW loci were connected, they were given an increased prior for both being plausible candidates. We also applied protein-protein interaction (PPI) analysis (see below for details) to all genes within 300 kb of each lead BW SNPs and ranked the genes based on the score for connectivity with the surrounding genes.

Evaluation of imputation quality of low-frequency variant at the *YKT6-GCK* locus. At the *YKT6-GCK* locus, the lead SNP (rs138715366) is of low-frequency in European ancestry populations (MAF=0.92%) and even rarer in other ancestry groups (MAF=0.23% in African Americans, otherwise monomorphic) and is not present in the HapMap reference panel[61]. To assess the accuracy of imputation for this low-frequent variant, we genotyped rs138715366 in the Northern Finland Birth Cohort (NFBC) 1966 (**Supplementary Table 1**). Of the 5,009 samples in the study, 4,704 were successfully imputed and genotyped (or sequenced) for rs138715366. The overall concordance rate between imputed and directly assayed genotypes was 99.8% and for directly assayed heterozygote calls was 75.0%.

Fine-mapping analyses. We sought to leverage LD differences between populations contributing to the trans-ancestry meta-analysis and to take advantage of the improved coverage of common and low-frequency variation offered by 1000G or 1000G and UK10K combined imputation to localise variants driving each distinct association signal achieving locus-wide significance. For each distinct signal, we used MANTRA[62] to construct 99% credible sets of variants[63] that together account for 99% of the posterior probability of driving the association. MANTRA incorporates a prior model of relatedness between studies, based on mean pair-wise allele frequency differences across loci, to account for heterogeneity in allelic effects (**Supplementary Table 3**). MANTRA has been demonstrated, by simulation, to improve localisation of causal variants compared with either a fixed- or random-effects trans-ancestry meta-analysis[62,64].

For loci with only one signal of association, we used MANTRA to combine summary statistics from the six non-European GWAS and the two European ancestry components. However, for loci with multiple distinct association signals, we used MANTRA to combine summary statistics from approximate conditioning for the two European components, separately for each signal.

For each distinct signal, we calculated the posterior probability that the *j*th variant, π_{Cj}, is driving the association, given by

$$\pi_{\mathrm{C}j} = \frac{\Lambda_j}{\sum_k \Lambda_k},$$

where the summation is over all variants mapping within the (conditional) meta-analysis across the locus. In this expression, Λ_j is the Bayes' factor (BF) in favour of association from the MANTRA analysis. A 99% credible set[63] was then constructed by: (i) ranking all variants according to their BF, Λ_j; and (ii) including ranked variants until their cumulative posterior probability exceeds 0.99.

Genomic annotation. We used genomic annotations of DNaseI hypersensitive sites (DHS) from the ENCODE[65] project and protein coding genes from GENCODE[66]. We filtered cell types that are cancer cell lines (karyotype 'cancer' from https://genome.ucsc.edu/ENCODE/cellTypes.html), and merged data from multiple samples from the same cell type. This resulted in 128 DHS cell-type annotations, as well as 4 gene-based annotations (coding exon, 5UTR, 3UTR and 1kb upstream of TSS). First, we tested for the effect of each cell type DHS and gene annotation individually using the Bayes' factors for all variants in the 62 credible sets using fgwas[67]. Second, we categorised the annotations into 'genic', 'foetal DHS', 'embryonic DHS', 'stem cell DHS', 'neonatal DHS' and 'adult DHS' based on the description fields from ENCODE, and tested for the effect of each category individually as described above using fgwas. Third, we then tested the effect of each category by including all categories in a joint model using fgwas. For each of the three analyses, we obtained the estimated effects and 95% confidence intervals (CI) for each annotation, and considered an annotation enriched if the 95% CI did not overlap zero.

Estimation of genetic variance explained. Variance explained was calculated using the REML method implemented in GCTA[68]. We considered the variance explained by two sets of SNPs: (i) lead SNPs of all 62 distinct association signals at the 59 established and novel autosomal BW loci identified in the European-specific or trans-ancestry meta-analyses; (ii) lead SNPs of 55 distinct association signals at the 52 novel autosomal BW loci (**Extended Data Table 1a** and **Supplementary Table 7**). Variance explained was calculated in samples of European ancestry in the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study[69] (independent of the meta-analysis) and two studies that were part of the European ancestry meta-analysis: NFBC1966 and Generation R (**Supplementary Table 1**). In each study, the genetic relationship matrix was estimated for each set of SNPs and was tested individually against BW (males and females combined) with study specific covariates. These analyses provided an estimate and standard error for the variance explained by each of the given sets of SNPs.

Examining the relative effects on BW of maternal and foetal genotype at the 60 identified loci. We performed four sets of analyses.

First, we used GWAS data from 4,382 mother-child pairs in the Avon Longitudinal Study of Parents and Children (ALSPAC) study to fit a "maternal-GCTA model"[6] to estimate the extent to which the maternal genome might influence offspring BW independent of the foetal genome. The m-GCTA model uses genome-wide genetic similarity between mothers and offspring to partition the phenotypic variance in BW into components due to the maternal genotype, the child's genotype, the covariance between the two and environmental sources of variation.

Second, we compared associations with BW of the foetal versus maternal genotype at each of the 60 BW loci. The maternal allelic effect on offspring BW was obtained from a maternal GWAS meta-analysis of 68,254 European mothers from the EGG Consortium (n=19,626)[7] and the UK Biobank (n=48,628). In the UK Biobank, mothers were asked to report the BW of their first child. Women of European ancestry with genotype data available in the May 2015 data release were included, and those with reported BW equivalent to <2.5 kg or >4.5 kg were excluded. No

information on gestational age or gender of child was available. BW of first child was associated with maternal factors such as smoking status, BMI and height in the expected directions. Of the 68,254 women included in the maternal GWAS, 13% were mothers of individuals included in the current foetal European ancestry GWAS, and a further approximately 45% were themselves (with their own BW) included in the foetal GWAS.

Third, we additionally conducted analyses in 12,909 mother-child pairs from nine contributing studies: at each of the 60 loci, we compared the effect of the foetal genotype on BW adjusted for sex and gestational age, with and without adjustment for maternal genotype. We reciprocally compared the association between the maternal genotype and BW with and without adjustment for foetal genotype.

Fourth, we used the method of Zhang et al[15] to test associations between BW and the maternal untransmitted, maternal transmitted and inferred paternal transmitted haplotype score of 422 height SNPs[25], 30 SBP SNPs[13,14] and 84 T2D SNPs[24] in 5,201 mother-child pairs from the ALSPAC study.

LD Score Regression. The use of LD Score regression to estimate the genetic correlation between two traits/diseases has been described in detail elsewhere[70]. Briefly, "LD Score" is a measure of how much genetic variation each variant tags; if a variant has a high LD Score then it is in high LD with many nearby polymorphisms. Variants with high LD Scores are more likely to contain more true signals and hence provide more chance of overlap with genuine signals between GWAS. The LD score regression method uses summary statistics from the GWAS meta-analysis of BW and the other traits of interest, calculates the cross-product of test statistics at each SNP, and then regresses the cross-product on the LD Score. Bulik-Sullivan et al[70] show that the slope of the regression is a function of the genetic covariance between traits:

$$E\left(z_{1j}z_{2j}\right) = \frac{\sqrt{N_1N_2}\rho_g}{M} l_j + \frac{\rho N_s}{\sqrt{N_1N_2}}$$

where N_i is the sample size for study i, ρ_g is the genetic covariance, M is the number of SNPs in the reference panel with MAF between 5% and 50%, l_j is the LD score for SNP j, N_s quantifies the number of individuals that overlap both studies, and ρ is the phenotypic correlation amongst the N_s overlapping samples. Thus, if there is sample overlap (or cryptic relatedness between samples), it will only affect the intercept from the regression (i.e. the term $\frac{\rho N_s}{\sqrt{N_1N_2}}$) and not the slope, and hence estimates of the genetic covariance will not be biased by sample overlap. Likewise, population stratification will affect the intercept but will have minimal impact on the slope (i.e. intuitively since population stratification does not correlate with linkage disequilibrium between nearby markers).

Summary statistics from the GWAS meta-analysis for traits and diseases of interest were downloaded from the relevant consortium website. The summary statistics files were reformatted for LD Score regression analysis using the munge_sumstats.py python script provided on the developer's website (https://github.com/bulik/ldsc). For each trait, we filtered the summary statistics to the subset of HapMap 3 SNPs[71], as advised by the developers, to ensure that no bias was introduced due to poor imputation quality. Summary statistics from the European-specific BW meta-analysis were used because of the variable LD structure between ancestry groups. Where the sample size for each SNP was included in the results file this was flagged using --N-col; if no sample size was available then the maximum sample size reported in the reference for the GWAS meta-analysis was used. SNPs were excluded for the following reasons: MAF<0.01; ambiguous strand; duplicate rsID; non-autosomal SNPs; reported sample size less than 60% of the total available. Once all files were reformatted, we used the ldsc.py python script, also on the developers' website, to calculate the genetic correlation between BW and each of the traits and diseases. The European LD Score files

that were calculated from the 1000G reference panel and provided by the developers were used for the analysis. Where multiple GWAS meta-analyses had been conducted on the same phenotype (i.e. over a period of years), the genetic correlation with BW was estimated using each set of summary statistics and presented in **Supplementary Table 12**. The phenotypes with multiple GWAS included height, BMI, waist-hip ratio (adjusted for BMI), total cholesterol, triglycerides, high density lipoprotein (HDL) and low density lipoprotein (LDL). The estimate of the genetic correlation between the multiple GWAS meta-analyses on the same phenotype were comparable and the later GWAS had a smaller standard error due to the increased sample size, so only the genetic correlation between BW and the most recent meta-analyses were presented in **Fig. 2**.

In the published GWAS for BP[14] the phenotype was adjusted for BMI. Caution is needed when interpreting the genetic correlation between BW and BMI-adjusted SBP due to the potential for collider bias[72]. Since BMI is associated with both BP and BW, it is possible that the use of a BP genetic score adjusted for BMI might bias the genetic correlation estimate towards a more negative value. To verify that the inverse genetic correlation with BW (r_g=-0.26, SE=0.05, P=6.5x10^{-9}) was not due to collider bias caused by the BMI adjustment of the phenotype, we obtained an alternative estimate using UK Biobank GWAS data for SBP that was unadjusted for BMI and obtained a similar result (r_g=-0.22, SE=0.03, P=5.5x10^{-13}). The SBP phenotype in UK Biobank was prepared as follows. Two BP readings were taken at assessment, approximately 5 minutes apart. We included all individuals with an automated BP reading (taken using an automated Omron BP monitor). Two valid measurements were available for most participants (averaged to create a BP variable, or alternatively a single reading was used if only one was available). Individuals were excluded if the two readings differed by more than 4.56 SD. BP measurements more than 4.56 SD away from the mean were excluded. We accounted for BP medication use by adding 15 mmHg to the SBP measure. BP was adjusted for age, sex and centre location and then inverse rank normalised. We performed the GWAS on 127,698 individuals of British descent using BOLT-LMM[37], with genotyping array as covariate.

Estimating the proportion of the BW-adult traits covariance attributable to genotyped SNPs. We estimated the phenotypic, genetic and residual correlations as well as the genetic and residual covariance between BW and several quantitative traits/disease outcomes in UK Biobank using directly genotyped SNPs and the REML method implemented in BOLT-LMM[37]. The traits examined included T2D, SBP, diastolic BP, CAD, height, BMI, weight, waist-hip ratio, hip circumference, waist circumference, obesity, overweight, age at menarche, asthma, and smoking. Where phenotypes were not available (e.g. serum blood measures are not currently available in UK Biobank), we obtained estimates using the NFBC1966 study (for correlations/covariance between BW and triglycerides, total cholesterol, HDL, LDL, fasting glucose and fasting insulin). In the UK Biobank analysis, we used 57,715 unrelated individuals with BW available and identified by UK Biobank as white British. SNPs with evidence of deviation from Hardy-Weinberg Equilibrium (P<1x10^{-6}), MAF<0.05 or overall missing rate >0.015 were excluded, resulting in 328,928 SNPs for analysis. We included the first five ancestry principal components as covariates. In the NFBC1966 analysis, 5,009 individuals with BW were enrolled. Genotyped SNPs that passed quality control (**Supplementary Table 2**) were included, resulting in 324,895 SNPs for analysis. The first three ancestry principal components and sex were included as covariates.

Gene set enrichment analysis. Meta-Analysis Gene-set Enrichment of variaNT Associations (MAGENTA) was used to explore pathway-based associations using summary statistics from the trans-ancestry meta-analysis. MAGENTA implements a gene set enrichment analysis (GSEA) based approach, as previously described[9]. Briefly, each gene in the genome is mapped to a single index SNP with the lowest *P*-value within a 110 kb upstream and 40 kb downstream window. This *P*-value, representing a gene score, is then corrected for confounding factors such as gene size, SNP density and LD-related properties in a regression model. Genes within the HLA-region were excluded from

analysis due to difficulties in accounting for gene density and LD patterns. Each mapped gene in the genome is then ranked by its adjusted gene score. At a given significance threshold (95th and 75th percentiles of all gene scores), the observed number of gene scores in a given pathway, with a ranked score above the specified threshold percentile, is calculated. This observed statistic is then compared to 1,000,000 randomly permuted pathways of identical size. This generates an empirical GSEA *P*-value for each pathway. Significance was attained when an individual pathway reached a false discovery rate (FDR) <0.05 in either analysis. In total, 3,216 pre-defined biological pathways from Gene Ontology, PANTHER, KEGG and Ingenuity were tested for enrichment of multiple modest associations with BW. The MAGENTA software was also used for enrichment testing of custom gene sets.

Protein-Protein interaction network analyses. We used the integrative Protein-Interaction-Network-Based Pathway Analysis (iPINBPA) method[73]. Briefly, we generated gene-wise *P*-values from the trans-ancestry meta-analysis using VEGAS2[74], which map the SNPs to genes and account for possible cofounders, such as LD between markers. The empirical gene-wise *P*-values are calculated using simulations from the multivariate normal distribution. Those that were nominally significant ($P \leq 0.01$) were selected as "seed genes", and were collated within high confidence version of inweb3[75], to weight the nodes in the network following a guilt-by-association approach. In a second step, a network score was defined by the combination of the *z*-scores derived from the gene-wise *P*-values with node weights using the Liptak-Stouffer method[76]. A heuristic algorithm was then applied to extensively search for modules enriched in genes with low *P*-values. The modules were further normalised using a null distribution of 10,000 random networks. Only those modules with *z*-score >5 were selected. Finally, the union of all modules constructed a BW-overall PPI network. Both the proteins on the individual modules and on the overall BW-PPI were interrogated for enrichment in Gene Ontology Terms (Biological Processes) using a Hypergeometric test. Terms were considered as significant when adjusted *P*-value, following Benjamini-Hochberg procedure, was below 0.05.

Point of contact (PoC) analyses. The same methodology described above was applied to 16 different adult traits resulting in a number of enriched modules per trait. Different modules for each trait were combined in a single component and the intersection between these trait-specific components and the BW component was calculated. This intersection is defined as the PoC network. We used the resulting PoC networks in downstream analyses to interrogate which set of proteins connects BW variation and adult trait variation via pathways enriched in the overall BW analysis.

Parent-of-origin specific associations. We first searched for evidence of parent of origin effects in the UK Biobank samples by comparing variance between heterozygotes and homozygotes using Quicktest[77]. In this analysis, we used only unrelated individuals identified genetically as of white British origin (n=57,715). Principal components were generated using these individuals and the first five were used to adjust for population structure as covariates in the analysis, in addition to a binary indicator for genotyping array.

We also examined 4,908 mother-child pairs in ALSPAC and determined the parental origin of the alleles where possible[78]. Briefly, the method uses mother-child pairs to determine the parent of origin of each allele. For example, if the mother/child genotypes are AA/Aa, the child's maternal/paternal allele combination is A/a. For the situation where both mother and child are heterozygous, the child's maternal/paternal alleles cannot be directly specified. However, the parental origin of the alleles can be determined by phasing the genotype data and comparing maternal and child haplotypes. We then tested these alleles for association with BW adjusting for sex and gestational age.

Statistical power in these currently available sample sizes is insufficient to rule out widespread parent-of-origin effects across the regions tested. Using the mean beta (0.034 SD) and MAF (0.28) of the identified loci, we estimate that we would need at least 200,000 unrelated

individuals or 70,000 mother-child pairs for 80% power to detect parent-of-origin effects at P<0.00085.

Hierarchical clustering of BW loci. To explore the different patterns of association between BW and other anthropometric/metabolic/endocrine traits and diseases, we performed hierarchical clustering analysis. The lead SNP (or proxy, EUR r^2>0.6) at the 60 BW loci was queried in publicly available GWAS meta-analysis datasets or in GWAS result obtained through collaboration[79]. Results were available for 53 of those loci and the extracted *z*-score (allelic effect/SE, **Supplementary Table 17**) was aligned to the BW-raising allele. We performed two dimensional clustering by trait and by locus. We computed the Euclidean distance amongst *z*-scores of the extracted traits/loci and performed complete hierarchical clustering implemented in the pvclust package (http://www.sigmath.es.osaka-u.ac.jp/shimo-lab/prog/pvclust/) in R v3.2.0 (http://www.R-project.org/). Clustering uncertainty was measured by multiscale bootstrap resampling estimated from 1,000 replicates. We used α=0.05 to define distinct clusters and, based on the bootstrap analysis, calculated the Calinski index to identify the number of well-supported clusters (cascadeKM function, Vegan package, http://CRAN.R-project.org/package=vegan). Clustering was visualised by constructing dendrograms and a heatmap.

Separately from the hierarchical clustering analysis, we queried the lead SNP at *EPAS1* in a GWAS of haematological traits[80] because variation at that locus has previously been implicated in BW and adaptation to hypoxia at high altitudes in Tibetans[81,82] (**Supplementary Table 17**).

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ENDNOTES

Supplementary Information is linked to the online version of the paper.

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Author Information

Summary statistics from the meta-analyses are available at http://egg-consortium.org/. Reprints and permissions information is available at www.nature.com/reprints. One of the authors discloses competing financial interests: Krina Zondervan has a scientific collaboration with Bayer HealthCare Ltd. and Population Diagnostics Inc. Correspondence and requests for materials should be addressed to mark.mccarthy@drl.ox.ac.uk and r.freathy@ex.ac.uk.

EXTENDED DATA LEGENDS

Extended Data Figure 1 | Flow chart of the study design.

Extended Data Figure 2 | Manhattan and quantile-quantile (QQ) plots of the trans-ancestry meta-analysis for birth weight. a, Manhattan (main panel) and QQ (top right) plots of genome-wide association results for BW from trans-ancestry meta-analysis of up to 153,781 individuals. The association *P*-value (on -$\log_{10}$ scale) for each of up to 22,434,434 SNPs (*y* axis) is plotted against the genomic position (NCBI Build 37; *x* axis). Association signals that reached genome-wide significance ($P<5x10^{-8}$) are shown in green if novel and pink if previously reported. In the QQ plot, the black dots represent observed *P*-values and the grey line represents expected *P*-values under the null distribution. The red dots represent observed *P*-values after excluding the previously identified signals[5]. **b,** Manhattan (main panel) and QQ (top right) plots of trans-ethnic GWAS meta-analysis for BW highlighting the reported imprinted regions described in Supplementary Table 14. Novel association signals that reached genome-wide significance ($P<5x10^{-8}$) and mapped to imprinted regions are shown in green. Genomic regions outside imprinted regions are shaded in grey. SNPs in the imprinted regions are shown in light blue or dark blue, depending on chromosome number (odd or even). In the QQ plot, the black dots represent observed *P* values and the grey lines represent expected *P*-values and their 95% confidence intervals under the null distribution for the SNPs within the imprinted regions.

Extended Data Figure 3 | Regional plots for multiple distinct signals at three birth weight loci, *ZBTB7B* (a), *HMGA1* (b) and *PTCH1* (c). Regional plots for each locus are displayed from: the unconditional European-specific meta-analysis of up to 143,677 individuals (left); the approximate conditional meta-analysis for the primary signal after adjustment for the index variant for the secondary signal (middle); and the approximate conditional meta-analysis for the secondary signal after adjustment for the index variant for the primary signal (right). Directly genotyped or imputed SNPs are plotted with their association *P*-values (on a -$\log_{10}$ scale) as a function of genomic position (NCBI Build 37). Estimated recombination rates (blue lines) are plotted to reflect the local LD structure around the index SNPs and their correlated proxies. SNPs are coloured in reference to LD with the particular index SNP according to a blue to red scale from r^2 = 0 to 1, based on pairwise r^2 values estimated from a reference of 5,000 individuals of white British origin, randomly selected from the UK Biobank.

Extended Data Figure 4 | Comparison of foetal effect sizes and maternal effect sizes at 60 known and novel birth weight loci (continues to Extended Data Figure 5). For each BW locus, the following six effect sizes (with 95% CI) are shown, all aligned to the same BW-raising allele: **foetal_GWAS** = foetal allelic effect on BW (from European ancestry meta-analysis of up to n=143,677 individuals); **foetal_unadjusted** = foetal allelic effect on BW (unconditioned in n=12,909 mother-child pairs); **foetal_adjusted** = foetal effect (conditioned on maternal genotype, n=12,909); **maternal_GWAS** = maternal allelic effect on offspring BW (from meta-analysis of up to n=68,254 European mothers)[7]; **maternal_unadjusted** = maternal allelic effect on offspring BW (unconditioned, n=12,909); **maternal_adjusted** = maternal effect (conditioned on foetal genotype, n=12,909). The 60 BW loci are ordered by chromosome and position (Supplementary Tables 10, 11). These plots illustrate that in large GWAS of BW, foetal effect size estimates are larger than those of maternal at 55/60 identified loci (binomial $P=1x10^{-11}$), suggesting that most of the associations are driven by the foetal genotype. In conditional analyses that modelled the effects of both maternal and foetal genotypes (n=12,909 mother-child pairs), confidence intervals around the estimates were wide, precluding inference about the likely contribution of maternal vs. foetal genotype at individual loci.

Extended Data Figure 5 | Comparison of foetal effect sizes and maternal effect sizes at 60 known and novel birth weight loci. a, Continued from Extended Data Figure 4. **b,** The scatterplot illustrates the difference between the foetal (*x* axis) and maternal (*y* axis) effect sizes in the overall maternal vs. foetal GWAS results.

Extended Data Figure 6 | Protein-Protein Interaction (PPI) Network analysis. a, Illustrates the largest global component of birth weight (BW) PPI network containing 13 modules. **b,** The histogram shows the null distribution of z-scores of BW PPI networks based on 10,000 random networks, and where the z-scores for the 13 BW modules (M1-13) lie. For each module, the two most significant GO terms are depicted. **c,** Illustrates a heatmap which takes the top 50 biological processes over-represented in the global BW PPI network (listed at the right of the plot), and displays extent of enrichment for the various trait-specific "point of contact" (PoC) PPI networks. **d-e,** Trait-specific PoC PPI networks composed of proteins that are shared in both the global BW PPI network and networks generated using the same pipeline for each of the adult traits: **d,** canonical Wnt signalling pathway enriched for PoC PPI between BW and blood pressure (BP)-related phenotypes; and **e,** regulation of insulin secretion pathway enriched for PoC between BW and type 2 diabetes (T2D)/fasting glucose (FG). Red nodes are those that are present in PoC for BW and traits of interest; blue nodes correspond to the pathway nodes; purple nodes are those present in both the pathway and PoC; orange nodes are genes in BW loci that overlap with both the pathway and PoC. Large nodes correspond to genes in BW loci (within 300kb from the lead SNP), and have black border if they, amongst all BW loci, have a stronger (top 5) association with at least one of the pairing adult traits.

Extended Data Figure 7 | Quantile-Quantile (QQ) plots of (a) variance comparison between heterozygotes and homozygotes analysis in 57,715 UK Biobank samples and (b) parent-of-origin specific analysis in 4,908 ALSPAC mother-child pairs at 59 autosomal birth weight loci plus *DLK1*. a, QQ plot from the Quicktest[77] analysis comparing the BW variance of heterozygotes with homozygotes in 57,715 UK Biobank samples. **b,** QQ plot from the parent-of-origin specific analysis testing the association between BW and maternally transmitted vs. paternally transmitted alleles in 4,908 mother-child pairs from the ALSPAC study (Methods, Supplementary Tables 15, 16). In both panels, the black dots represent lead SNPs at 59 identified autosomal BW loci and a further sub-genome-wide significant signal for BW near *DLK1* (rs6575803; P=5.6x10^{-8}). The grey lines represent expected *P* values and their 95% confidence intervals under the null distribution for the 60 SNPs. Both results show trends in favour of imprinting effects at BW loci: however, despite the large sample size, these analyses were underpowered (see Methods) and much larger sample sizes are required for definitive analysis.

Extended Data Figure 8 | Summary of previously reported loci for systolic blood pressure (SBP, a), coronary artery disease (CAD, b, e), type 2 diabetes (T2D, c, f) and adult height (d) and their effect on birth weight. a-d, Effect sizes (left *y* axis) of previously reported 30 SBP loci[13,14], 45 CAD loci[23], 84 T2D loci[24] and 422 adult height loci[25] are plotted against effects on BW (*x* axis). Effect sizes are aligned to the adult trait-raising allele. The colour of each dot indicates BW association *P* value: red, $P<5\times10^{-8}$; orange, $5\times10^{-8}\leq P<0.001$; yellow, $0.001\leq P<0.01$; white, $P\geq0.01$. The superimposed grey frequency histogram shows the number of SNPs (right *y* axis) in each category of BW effect size. **e,** Effect sizes (with 95% CI) on BW of 45 known CAD loci are plotted arranged in the order of CAD effect size from highest to lowest, separating out the known SBP loci. CAD loci with a larger effect on BW concentrated amongst loci with primary BP association. **f,** Effect sizes (with 95% CI) on BW of 32 known T2D loci are plotted, subdivided by previously reported categories derived from detailed adult physiological data[27]. Heterogeneity in BW effect sizes between five T2D loci groups with different mechanistic categories was substantial (P_{het}=1.2x10^{-9}). In pairwise comparisons, the "beta cell" group of variants differed from the other four groups: fasting hyperglycaemia (P_{het} =3x10^{-11}),

insulin resistance (P_{het} =0.002), proinsulin (P_{het} =0.78) and unclassified (P_{het} =0.02) groups. All of the BW effect sizes plotted in the forest plots are aligned to the trait (or risk)-raising allele.

Extended Data Table 1 | Sixty loci associated with birth weight ($P<5x10^{-8}$) in European ancestry meta-analysis of up to 143,677 individuals and/or trans-ancestry meta-analysis of up to 153,781 individuals. a, Effects (beta values) are aligned to the BW-raising allele. EAF was obtained from the trans-ancestry meta-analysis, except for *PLAC1*, for which the EAF was obtained from the European ancestry meta-analysis due to lack of X chromosome data from the non-European studies. Chr., chromosome; bp, base pair; EAF, effect allele frequency; SE, standard error. **b,** The effect of the lead SNP (absolute value of beta, *y* axis) is given as a function of minor allele frequency (*x* axis) for 60 known (pink) and novel (green) BW loci from the trans-ancestry meta-analysis. Error bars are proportional to the standard error of the effect size. The dashed line indicates 80% power to detect association at genome-wide significance level for the sample size in trans-ancestry meta-analysis.

Extended Data Table 2 | Gene set enrichment analysis and protein-protein interaction (PPI) analysis. Two complementary analyses of the overall GWAS summary data identified enrichment of BW associations in biological pathways related to metabolism, growth and development. **a,** The top results (FDR<0.05 at the 95th percentile enrichment threshold) from a total of 3,216 biological pathways tested for enrichment of multiple modest associations with BW. Additionally, results are presented for custom sets of imprinted genes. **b,** The results of a complementary analysis of empirical PPI data, displaying the top 10 most significant pathways enriched for BW-association scores.

Contents of Supplementary Information

1. Supplementary Tables and Notes

These tables and notes are provided in this document.

2. Supplementary Data

These table (excel spreadsheet) and plots (pdf file) are provided in separate documents.

- Supplementary Table 17 Association of BW signals with various adult metabolic and anthropometric traits. (GWAS look-ups)
- 60 regional plots for birth weight association

Supplementary Table 1. Description of studies contributing to trans-ancestry meta-analysis: ancestry group and country of origin, sample size, data collection methods, and birth weight summaries and exclusions.

(a) Component 1: European ancestry GWAS

Study	Ancestry group	Country of origin	Year(s) of birth	Sample size (M/F)	Data collection	Phenotype exclusions	Mean (SD) birth weight (grams)			Median (IQR) GA (week) at delivery
							Males	Females	Combined	
1958 British Birth Cohort	European	UK	1958	4,595 (2,320/2,275)	Measured by midwives; supplemented with obstetric records and interviews with mothers	Multiple births, GA <37 weeks	3439 (484)	3277 (468)	3359 (483)	40 (39-41)
ALSPAC[a,b]	European	UK	~1992	7,285 (3,722/3,563)	Identified from obstetric data, records from the ALSPAC measurers, and birth notification	Multiple births, GA <37 weeks, 5 SD winsorisation	3553 (491)	3423 (450)	3490 (476)	40 (40-41)
CHOP-Caucasian	European	USA	1988-present	9,405 (5,040/4,365)	Questionnaire and medical records	Multiple births, GA <37 weeks (when available)	3447 (582)	3343 (549)	3398 (569)	N/A
CoLaus	European	Switzerland	1928-1970	2,089 (892/1,197)	Self-reported as adults	N/A	3490 (668)	3250 (661)	3352 (675)	N/A
COPSAC-2000	European	Denmark	1998-2001	352 (173/179)	Medical records	Multiple births, GA <37 weeks	N/A	N/A	3555 (485)	40 (39-41)
COPSAC-2010	European	Denmark	2008-2011	589 (306/283)	Medical records	Multiple births, GA <37 weeks	3635 (483)	3536 (474)	3588 (481)	40 (39-41)
COPSAC-REGISTRY	European	Denmark	1987-1999	1,210 (804/406)	Medical Records	Multiple births, GA <37 weeks	3609 (498)	3443 (447)	3553 (488)	40 (39-41)
DNBC	European	Denmark	1996-2003	915 (475/440)	Danish Medical Birth Register	Multiple births, GA <37 weeks, congenital abnormalities	3767 (480)	3625 (443)	3699 (468)	40 (40-41)
ERF	European	Netherlands	Various	459 (187/272)	Interview	GA <37 weeks	3161 (680)	2955 (608)	3039 (644)	N/A
EPIC	European	UK	1993-1997	8,939 (3,448/5,491)	Self-reported	N/A	3505 (786)	3266 (750)	3358 (772)	N/A
Fenland (GA+)	European	UK	1950-1975	5,188 (2,088/3,100)	Self-reported as adults	GA described as "very pre-term" or "pre-term"	3433 (638)	3260 (594)	3394 (555)	N/A
Fenland (GA-)	European	UK	1950-1975	833 (509/324)	Self-reported as adults	None	3465 (593)	3154 (608)	3354 (624)	N/A
Generation R	European	Netherlands	2002-2006	2,701 (1,378/1,323)	Hospital records and community midwives	Multiple births, GA <37 weeks	3628 (494)	3518 (475)	3574 (488)	40 (39-41)
GINIplus & LISAplus (GA+)	European	Germany	1996-1999	656 (360/296)	Parental report of medical records	Multiple births, GA <37 weeks, <2500g	3498 (406)	3376 (417)	3443 (415)	40 (39-41)

Study	Ancestry group	Country of origin	Year(s) of birth	Sample size (M/F)	Data collection	Phenotype exclusions	Mean (SD) birth weight (grams)			Median (IQR) GA (week) at delivery
							Males	Females	Combined	
GINIplus & LISAplus (GA-)	European	Germany	1996-1999	790 (391/399)	Parental report of medical records	Multiple births, GA <37 weeks, <2500g	3499 (429)	3348 (423)	3423 (433)	N/A
GOYA	European	Denmark	1943-1952	149/0 (obese), 141/0 (control)	School health records	N/A	N/A	N/A	3553 (711)	N/A
HBCS	European	Finland	1934-1944	1472 (639/833)	Birth records	Multiple births, GA <37 weeks	3536 (460)	3375 (439)	3444 (454)	40 (39-41)
INMA	European	Spain	1997-2006	1,021 (527/494)	Well-trained midwives and nurses	None	3362 (406)	3188 (422)	3278 (423)	40 (39-41)
INTER99	European	Denmark	1939-1969	4,243 (1,981/2,262)	Measured by midwives and obtained from obstetric record registry	Multiple births, GA <37 weeks	3505 (493)	3370 (469)	3433 (485)	N/A
Leipzig	European	Germany	1985 - 2010	597 (304/293)	Questionnaire to mothers, documentation of medical screening examination if available	GA <37 weeks	3573 (531)	3480 (538)	3527 (536)	40 (39-40)
NEO	European	Netherlands	1943-1963	504 (exact; 200/304), 3215 (range; 1,450/1,765)	Questionnaire	N/A	3669 (1068)	3236 (973)	3514 (1271)	N/A
NFBC1966	European	Finland	1966	5,009 (2,393/2,616)	Measured in hospitals	Multiple births, GA <37 weeks or unknown	3607 (506)	3480 (466)	3541 (489)	40 (39-41)
NFBC1986	European	Finland	1986	4,680 (2,306/2,374)	Measured in hospitals	Multiple births, GA <37 weeks or unknown	3626 (543)	3519 (521)	3572 (535)	40 (39-40)
NTR	European	Netherlands	1926-1998	1,265 (447/818)	Parental report or self-reported	Multiple births, GA <37 weeks	3414 (619)	3544 (630)	3343 (601)	40 (40-40)
ORCADES	European	Scotland	1920-1991	960 (330/630)	Self-reported as adults	N/A	3401 (607)	3654 (685)	3488 (640)	N/A
PANIC	European	Finland	1999-2002	436 (231/205)	Medical records and parental questionnaire	Multiple births, GA <37 weeks	3646 (488)	3528 (444)	3588 (474)	40 (39-41)
RAINE	European	Australia	1989-1991	1,347 (693/654)	Recorded at delivery by study personnel or obtained from hospital reports	Multiple births, GA <37 weeks	3505 (471)	3390 (462)	3449 (470)	40 (39-41)
SORBS	European	Germany	1925-1988	298 (113/185)	Interview at recruitment	N/A	N/A	N/A	3393 (673)	N/A
STRIP	European	Finland	1989-1991	599 (311/288)	Medical records	Multiple births, GA <37 weeks	3696 (471)	3535 (443)	3619 (465)	40 (39-40)
TEENAGE (GA+)	European	Greece	1993-1998	279 (126/153)	Measured by midwives or paediatricians; supplemented with data from mothers' interviews	GA <37 weeks	3403 (467)	3280 (421)	3336 (445)	40 (38-40)
TEENAGE (GA-)	European	Greece	1993-1998	551 (234/317)	Measured by midwives or paediatricians; supplemented with data from mothers' interviews	N/A	3398 (459)	3298 (438)	3341 (449)	N/A
TDCOB-cases	European	Denmark	1987-2007	669	Measured by midwives and registered in	Multiple births	3682	3629	3660	40 (39-41)

				(391/278)	Danish Civil Registry		(536)	(545)	(540)	
TDCOB-controls	European	Denmark	1991-2006	560 (211/349)	Measured by midwives and registered in Danish Civil Registry	Multiple births	3627 (517)	3483 (485)	3540 (502)	40 (39-41)
YFS	European	Finland	1962-1977	1,915 (861/1,054)	Mothers' interview	Multiple births, GA >3 weeks pre-term	3648 (491)	3510 (451)	3572 (475)	N/A

(b) Component 2: UK BioBank

Study	**Ancestry group**	**Country of origin**	**Year(s) of birth**	**Sample size (M/F)**	**Data collection**	**Phenotype exclusions**	**Mean (SD) birth weight (grams)**			**Median (IQR) GA (weeks) at delivery**
							Males	**Females**	**Combined**	
UK BioBank	European	UK	2006-2010	67,786 (40,425/27,361)	Self-reported as adults	Multiple births, birth weight <2500g or >4000g	3452 (416)	3349 (417)	3391 (420)	N/A

(c) Component 3: Non-European ancestry GWAS

Study	**Ancestry group**	**Country of origin**	**Year(s) of birth**	**Sample size (M/F)**	**Data collection**	**Phenotype exclusions**	**Mean (SD) birth weight (grams)**			**Median (IQR) GA (weeks) at delivery**
							Males	**Females**	**Combined**	
CHOP-AA	African American	USA	1988-present	6,635 (3,343/3,292)	Questionnaire and medical records	Multiple births, GA <37 weeks (when available)	3276 (554)	3184 (535)	3231 (546)	N/A
CLHNS	Filipino	Philippines	1983-84	1,449 (755/694)	Local birth attendants	Multiple births, GA <37 weeks	3067 (401)	3018 (403)	3043 (403)	40 (38-40)
Generation R Turkish	Turkish	Netherlands	2002-2006	420 (215/205)	Hospital records and community midwives	Multiple births, GA <37 weeks	3477 (500)	3369 (415)	3424 (463)	40 (39-41)
Generation R Moroccan	Moroccan	Netherlands	2002-2006	365 (188/177)	Hospital records and community midwives	Multiple births, GA <37 weeks	3642 (447)	3417 (344)	3533 (416)	41 (40-41)
Generation R Surinamese	Surinamese	Netherlands	2002-2006	395 (215/180)	Hospital records and community midwives	Multiple births, GA <37 weeks	3288 (556)	3130 (490)	3216 (532)	40 (39-41)
SCORM	Chinese	Singapore	1992-1995	840 (420/420)	Documented medical record booklet	GA <37 weeks	3229 (422)	3182 (475)	3205 (450)	39 (38-40)

M, Males; F, Females; GA, gestational age; IQR, interquartile range; N/A, not applicable; SD, standard deviation.

[a]Boyd A, Golding J, Macleod J, Lawlor DA, Fraser A, et al. Cohort Profile: the 'children of the 90s'--the index offspring of the Avon Longitudinal Study of Parents and Children. *Int J Epidemiol* 42, 111-127 (2013).

[b]The study website contains details of all the data that is available through a fully searchable data dictionary (http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/).

Supplementary Table 2. Description of studies contributing to trans-ancestry meta-analysis: genotyping, quality control, pre-phasing, imputation, and association analysis.

(a) Component 1: European ancestry GWAS

Study	Genotyping array(s)[a]	Sample quality control		SNP scaffold quality control			Prephasing software	Imputation		Association analysis		Lambda (M/F)
		Call rate	Additional filters	Call rate	HWE *P*-value	Frequency		Software	Reference panel	Software	Covariates or adjustment	
1958 British Birth Cohort	I550, I610	None	Relatedness, ancestry outliers, sex discrepancy, identity, channel contrast	95%	$1x10^{-4}$	MAF<1%	MaCH	Minimac	1000G Mar 2012	ProbABEL	GA	1.01/1.00
ALSPAC	I550	97%	Heterozygosity, relatedness, ancestry outliers	95%	$5×10^{-7}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA, PC7	1.02/1.01
CHOP-Caucasian	I550, I610	95%	Relatedness, ancestry outliers, sex discrepancy	95%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	PC1-3	0.96/0.96
CoLaus	A5	90%	Relatedness, ancestry outliers	90%	$1x10^{-7}$	MAF<1%	MaCH	Minimac	1000G Mar 2012	In-house	None	0.99/1.00
COPSAC-2000	I550	97.5%	Heterozygosity, relatedness, ancestry outliers	98%	$1x10^{-6}$	MAF<0.1%	MaCH	Minimac	1000G Mar 2012	mach2qtl	GA	1.00/1.01
COPSAC-2010	IOEE	95%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy	95%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	QuickTest	GA, PC1-5	1.01/1.00
COPSAC-REGISTRY	IOEE	95%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy	97.5%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	QuickTest	GA, PC1-5	1.00/1.00
DNBC	I660	96%	Heterozygosity, ancestry outliers, sex discrepancy	98%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA	1.00/1.00
ERF	Various	98%	Relatedness, ancestry outliers, sex discrepancy	98%	$5x10^{-8}$	MAF<0.5%	MaCH	Minimac	1000G Mar 2012	ProbABEL	Kinship matrix	1.02/0.95
EPIC	AUKBB	97%	Heterozygosity, relatedness, sex discrepancy, singletons, channel contrast	95%	$1x10^{-6}$	MAC<1	SHAPEIT	IMPUTE2	1000G Mar 2012	SNPTEST	PC1-10	1.00/1.01
Fenland (GA+)	AUKBB	95%	Sex discrepancy, identity	95%	$1x10^{-6}$	MAC<2	SHAPEIT	IMPUTE2	1000G Mar 2012	SNPTEST	GA, PC1-10	1.00/1.01
Fenland (GA-)	AUKBB	95%	Sex discrepancy, identity	95%	$1x10^{-6}$	MAC<2	SHAPEIT	IMPUTE2	1000G Mar 2012	SNPTEST	PC1-10	0.99/1.00
Generation R	I610, I660	97.5%	Heterozygosity, ancestry outliers, sex discrepancy	98%	$1x10^{-6}$	MAF<1%	MaCH	Minimac	1000G Mar 2012	mach2qtl	GA, PC1-4	1.03/1.01
GINIplus & LISAplus	A5, A6	95%	Heterozygosity, ancestry outliers, sex discrepancy	95%	$1x10^{-5}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA	0.99/1.00
GOYA	I610	95%	Heterozygosity, ancestry outliers, sex discrepancy	95%	$1x10^{-7}$	MAF<1%	MaCH	MaCH	1000G Mar 2012	QuickTest	None	1.00/0.99
HBCS	I670	95%	Heterozygosity, relatedness, ancestry outliers	95%	$1x10^{-6}$	MAF<1%	MaCH	MaCH	1000G Mar 2012	mach2qtl	GA	1.02/1.02

Study	Genotyping array(s)[a]	Sample quality control		SNP scaffold quality control			Prephasing software	Imputation		Association analysis		Lambda (M/F)
		Call rate	Additional filters	Call rate	HWE *p*-value	Frequency		Software	Reference panel	Software	Covariates or adjustment	
INMA	IOQ	98%	Heterozygosity, relatedness, ancestry outliers, duplicates	95%	$1.1x10^{-6}$	MAF<1%	IMPUTE2	IMPUTE2	1000G Mar 2012	SNPTEST	GA	1.00/0.99
INTER99	ICM	95%	Relatedness, ancestry outliers, sex discrepancy	95%	$1x10^{-4}$	MAF<1%	IMPUTE2	IMPUTE2	1000G Mar 2012	SNPTEST	PC1	0.97/1.02
Leipzig	ICM	95%	Duplicates, ancestry outliers, sex discrepancy	95% (99% if MAF<5%)	$1x10^{-4}$	MAF<1%	IMPUTE2	IMPUTE2	1000G Mar 2012	SNPTEST	GA	0.95/0.96
NEO	ICE	98%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy	98%	$1x10^{-6}$	None	IMPUTE2	IMPUTE2	1000G Mar 2012	SNPTEST	PC1-5	0.99/0.99
NFBC1966	I370	95%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy, duplicates, withdrawn consent	95% (99% if MAF<5%)	$5.7x10^{-7}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA, PC1-3	1.00/0.99
NFBC1986	ICM	95%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy, duplicates, withdrawn consent	95% (99% if MAF<5%)	$5.7x10^{-7}$ ($1x10^{-4}$ if MAF<5%)	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA, PC1-3	1.00/1.10
NTR	A6, I370, I660, IOQ	90%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy	95%	$1x10^{-5}$	MAF<1%	MaCH	Minimac	1000G Mar 2012	PLINK	GA, array, PC1-6 (global), PC1-3 (local)	1.08/1.04
ORCADES	I300, IOQ, IOE	95%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy, duplicates	95% (99% if MAF<5%)	$1x10^{-6}$	MAF<1%	SHAPEIT	IMPUTE2	1000G Mar 2012	ProbABEL	array, PC1-3	1.00/0.99
PANIC	ICM, ICE	90 %	Heterozygosity, relatedness, ancestry outliers, sex discrepancy	95%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA, PC1-4	1.01/1.01
RAINE	I660	97%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy, chromosomal abnormalities	95%	$5.7x10^{-7}$	MAF<1%	MaCH	MaCH	1000G Mar 2012	ProbABEL	GA, PC1-2	1.01/0.99
SORBS	I660	94%	Relatedness, ancestry outliers, sex discrepancy, duplicates	95%	$1x10^{-4}$	MAF<1%	MaCH	Minimac	1000G Mar 2012	ProbABEL	Kinship matrix	1.01/1.01
STRIP	A5, A6	95%	Heterozygosity, ancestry outliers, twins	95%	$1x10^{-6}$	MAF<0.1%	SHAPEIT	IMPUTE2	1000G Mar 2012	SNPTEST	GA, PC1-4	1.01/1.01
TEENAGE (GA+)	ICM	95%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy	95% (99% if MAF<5%)	$1x10^{-4}$	MAF<1%	SHAPEIT	IMPUTE2	1000G Mar 2012	SNPTEST	GA	1.02/1.00
TEENAGE (GA-)	IOE	95%	Heterozygosity, relatedness, ancestry outliers, sex discrepancy	95% (99% if MAF<5%)	$1x10^{-4}$	MAF<1%	SHAPEIT	IMPUTE2	1000G Mar 2012	SNPTEST	None	1.02/0.98

TDCOB-cases	IOE	95%	Heterozygosity, relatedness, ancestry outliers	95%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA, PC1	1.02/1.01
TDCOB-controls	ICE	95%	Heterozygosity, relatedness, ancestry outliers	95%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA, PC1	1.02/1.05
YFS	I670	95%	Heterozygosity, relatedness, sex discrepancy, duplicates	95%	$1x10^{-6}$	MAF<1%	SHAPEIT	IMPUTE2	1000G Mar 2012	SNPTEST	PC1-4	0.99/1.01

(b) Component 2: UK BioBank

Study	**Genotyping array(s)[a]**	**Sample quality control**		**SNP scaffold quality control**			**Prephasing software**	**Imputation**		**Association analysis**		**Lambda**
		Call rate	**Additional filters**	**Call rate**	**HWE *P*-value**	**Frequency**		**Software**	**Reference panel**	**Software**	**Covariates or adjustment**	
UK BioBank	AUKBB	98%	Heterozygosity, relatedness, ancestry outliers	95%	N/A	MAF<1%	SHAPEIT2	IMPUTE2	1000G Oct 2014 & UK10K	BOLT-LMM	Sex, genotype array	N/A

(c) Component 3: Non-European ancestry GWAS.

Study	**Genotyping array(s)[a]**	**Sample quality control**		**SNP scaffold quality control**			**Prephasing software**	**Imputation**		**Association analysis**		**Lambda (M/F)**
		Call rate	**Additional filters**	**Call rate**	**HWE *P*-value**	**Frequency**		**Software**	**Reference panel**	**Software**	**Covariates or adjustment**	
CHOP-AA	I550, I610	95%	Relatedness, ancestry outliers, sex discrepancy	95%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	PC1-3	0.98/0.98
CLHNS	ICM	98.6%	Relatedness, sex discrepancy	97%	$1×10^{-6}$	N/A	MaCH	MaCH	1000G Mar 2012	mach2qtl	GA	1.02/1.02
Generation R Turkish	I610, I660	97.5%	Heterozygosity, ancestry outliers, sex discrepancy	95%	$1x10^{-7}$	MAF<1%	MaCH	Minimac	1000G Mar 2012	mach2qtl	GA, PC1-4	1.01/1.02
Generation R Moroccan	I610, I660	97.5%	Heterozygosity, ancestry outliers, sex discrepancy	90%	$1x10^{-7}$	MAF<1%	MaCH	Minimac	1000G Mar 2012	mach2qtl	GA, PC1-4	1.01/0.98
Generation R Surinamese	I610, I660	97.5%	Heterozygosity, ancestry outliers, sex discrepancy	98%	$1x10^{-7}$	MAF<1%	MaCH	Minimac	1000G Mar 2012	mach2qtl	GA, PC1	0.99/0.95
SCORM	I550	95%	Heterozygosity, relatedness, sex discrepancy	95%	$1x10^{-6}$	MAF<1%	SHAPEIT2	IMPUTE2	1000G Mar 2012	SNPTEST	GA	0.98/0.99

HWE, Hardy-Weinberg equilibrium; MAF, minor allele frequency; MAC, minor allele count; GA, gestational age; PC, principal component.
[a]Genotype array codes: Affymetrix 5.0 (A5); Affymetrix 6.0 (A6); Affymetrix Axiom UK BiLEVE (AUKBL); Affymetrix Axiom UK BioBank (AUKBB); Illumina Human370CNV (I370); Illumina HumanHap550 (I550); Illumina HumanHap610 (I610); Illumina HumanHap660 (I660); Illumina HumanHap670 (I670); Illumina CardioMetabochip (ICM); Illumina OmniQuad (IOQ); Illumina OmniExpress (IOE); Illumina CoreExome (ICE); Illumina OmniExpressExome (IOEE).

Supplementary Table 3. BW association summary statistics for each component of the trans-ancestry meta-analysis of 153,781 individuals for lead SNPs at loci attaining genome-wide significance ($P<5x10^{-8}$).

Locus: *WNT4-ZBTB40*. Lead SNP: rs2473248. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.86	0.039	0.008	$5.0x10^{-7}$	71,642	0.66
Component 2: UKBB	0.88	0.025	0.008	0.0032	67,786	N/A
European ancestry meta-analysis	0.87	0.033	0.006	$1.1x10^{-8}$	139,428	0.21
Component 3: non-European ancestry	0.78	0.039	0.018	0.034	8,653	0.43
Trans-ancestry meta-analysis	0.87	0.033	0.005	$1.1x10^{-9}$	148,081	0.72

Locus: *ZBTB7B*. Lead SNP: rs3753639. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.23	0.038	0.006	$3.9x10^{-9}$	70,376	0.60
Component 2: UKBB	0.25	0.024	0.006	0.00017	67,786	N/A
European ancestry meta-analysis	0.24	0.031	0.004	$7.3x10^{-12}$	138,162	0.12
Component 3: non-European ancestry	0.18	0.037	0.020	0.061	8,655	0.40
Trans-ancestry meta-analysis	0.23	0.031	0.004	$1.3x10^{-12}$	146,817	0.72

Locus: *FCGR2B*. Lead SNP: rs72480273. Effect/other alleles: C/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.16	0.029	0.007	$8.7x10^{-5}$	70,594	0.14
Component 2: UKBB	0.19	0.033	0.007	$2.3x10^{-6}$	67,786	N/A
European ancestry meta-analysis	0.17	0.031	0.005	$8.0x10^{-10}$	138,380	0.69
Component 3: non-European ancestry	0.15	0.005	0.023	0.84	8,655	0.71
Trans-ancestry meta-analysis	0.17	0.030	0.005	$1.5x10^{-9}$	147,035	0.86

Locus: *DTL*. Lead SNP: rs61830764. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.38	0.031	0.006	$1.0x10^{-7}$	70,372	0.12
Component 2: UKBB	0.38	0.013	0.006	0.019	67,786	N/A
European ancestry meta-analysis	0.38	0.022	0.004	$5.6x10^{-8}$	138,158	0.029
Component 3: non-European ancestry	0.15	0.016	0.024	0.50	8,655	0.30
Trans-ancestry meta-analysis	0.36	0.022	0.004	$4.5x10^{-8}$	146,813	0.18

Locus: *ATAD2B*. Lead SNP: rs7575873. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.88	0.040	0.008	$4.9x10^{-7}$	71,639	0.98
Component 2: UKBB	0.87	0.036	0.008	$6.3x10^{-6}$	67,786	N/A
European ancestry meta-analysis	0.88	0.038	0.006	$1.3x10^{-11}$	139,425	0.71
Component 3: non-European ancestry	0.93	-0.011	0.027	0.67	10,104	0.61
Trans-ancestry meta-analysis	0.88	0.036	0.006	$6.2x10^{-11}$	149,529	0.35

Locus: *EPAS1*. Lead SNP: rs1374204. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.70	0.050	0.006	$1.0x10^{-16}$	66,667	0.94
Component 2: UKBB	0.70	0.044	0.006	$9.7x10^{-14}$	67,786	N/A
European ancestry meta-analysis	0.70	0.047	0.004	$6.2x10^{-29}$	134,453	0.42
Component 3: non-European ancestry	0.63	0.031	0.016	0.049	8,654	0.14
Trans-ancestry meta-analysis	0.70	0.046	0.004	$1.5x10^{-29}$	143,107	0.82

Locus: *PTH1R*. Lead SNP: rs2242116. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.38	0.018	0.005	0.00048	75,884	0.48
Component 2: UKBB	0.38	0.025	0.006	$5.5x10^{-6}$	67,786	N/A
European ancestry meta-analysis	0.38	0.022	0.004	$1.4x10^{-8}$	143,670	0.37
Component 3: non-European ancestry	0.57	0.012	0.014	0.41	10,103	0.92
Trans-ancestry meta-analysis	0.39	0.021	0.004	$1.2x10^{-8}$	153,773	0.94

Locus: *ADCY5*. Lead SNP: rs11719201. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.22	0.052	0.006	$5.2x10^{-18}$	75,884	0.34
Component 2: UKBB	0.24	0.039	0.006	$4.0x10^{-10}$	67,786	N/A
European ancestry meta-analysis	0.23	0.046	0.004	$2.4x10^{-26}$	143,670	0.14
Component 3: non-European ancestry	0.13	0.037	0.022	0.095	9,264	0.18
Trans-ancestry meta-analysis	0.23	0.046	0.004	$6.4x10^{-27}$	152,934	0.35

Locus: *CPA3*. Lead SNP: rs10935733. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.42	0.023	0.005	$2.2x10^{-5}$	71,640	0.58
Component 2: UKBB	0.39	0.021	0.005	0.00012	67,786	N/A
European ancestry meta-analysis	0.41	0.022	0.004	$9.2x10^{-9}$	139,426	0.80
Component 3: non-European ancestry	0.60	0.038	0.015	0.013	10,103	0.62
Trans-ancestry meta-analysis	0.42	0.023	0.004	$6.2x10^{-10}$	149,529	0.33

Locus: *CCNL1-LEKR1*. Lead SNP: rs13322435. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.60	0.063	0.005	$1.0x10^{-30}$	71,640	0.0091
Component 2: UKBB	0.60	0.042	0.006	$3.4x10^{-13}$	67,786	N/A
European ancestry meta-analysis	0.60	0.053	0.004	$3.7x10^{-41}$	139,426	0.0080
Component 3: non-European ancestry	0.45	0.040	0.015	0.0066	10,103	0.66
Trans-ancestry meta-analysis	0.59	0.052	0.004	$1.3x10^{-42}$	149,529	0.14

Locus: *LCORL*. Lead SNP: rs925098. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.28	0.040	0.006	$4.8x10^{-12}$	71,640	0.46
Component 2: UKBB	0.26	0.027	0.006	$9.0x10^{-6}$	67,786	N/A
European ancestry meta-analysis	0.27	0.034	0.004	$5.4x10^{-16}$	139,426	0.11
Component 3: non-European ancestry	0.34	0.011	0.015	0.44	10,102	0.28
Trans-ancestry meta-analysis	0.28	0.032	0.004	$1.3x10^{-15}$	149,528	0.060

Locus: *HHIP*. Lead SNP: rs6537307. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.50	0.023	0.005	$1.5x10^{-5}$	71,645	0.35
Component 2: UKBB	0.49	0.029	0.005	$1.1x10^{-7}$	67,786	N/A
European ancestry meta-analysis	0.50	0.025	0.004	$9.5x10^{-12}$	139,431	0.41
Component 3: non-European ancestry	0.21	0.038	0.018	0.036	9,557	0.92
Trans-ancestry meta-analysis	0.48	0.026	0.004	$1.3x10^{-12}$	148,988	0.80

Locus: 5q11.2. Lead SNP: rs854037. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.81	0.038	0.007	$7.8x10^{-9}$	71,643	0.021
Component 2: UKBB	0.82	0.014	0.007	0.045	67,786	N/A
European ancestry meta-analysis	0.81	0.027	0.005	$2.2x10^{-8}$	139,429	0.011
Component 3: non-European ancestry	0.53	0.009	0.014	0.52	10,103	0.29
Trans-ancestry meta-analysis	0.80	0.025	0.005	$3.5x10^{-8}$	149,532	0.010

Locus: *EBF1*. Lead SNP: rs7729301. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.72	0.021	0.006	0.00035	75,883	0.23
Component 2: UKBB	0.74	0.027	0.006	$1.0x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.73	0.024	0.004	$1.6x10^{-8}$	143,669	0.48
Component 3: non-European ancestry	0.58	0.033	0.014	0.022	10,104	0.64
Trans-ancestry meta-analysis	0.72	0.025	0.004	$1.3x10^{-9}$	153,773	0.78

Locus: *CDKAL1*. Lead SNP: rs35261542. Effect/other alleles: C/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.72	0.047	0.006	$6.1x10^{-17}$	75,881	0.94
Component 2: UKBB	0.74	0.041	0.006	$1.4x10^{-11}$	67,786	N/A
European ancestry meta-analysis	0.73	0.044	0.004	$4.4x10^{-27}$	143,667	0.49
Component 3: non-European ancestry	0.75	0.044	0.016	0.0059	10,102	0.35
Trans-ancestry meta-analysis	0.73	0.044	0.004	$9.7x10^{-29}$	153,769	0.42

Locus: *HIST1H2BE*. Lead SNP: rs9379832. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.67	0.029	0.006	$7.2x10^{-7}$	70,375	1.0
Component 2: UKBB	0.73	0.016	0.006	0.011	67,786	N/A
European ancestry meta-analysis	0.70	0.023	0.004	$6.6x10^{-8}$	138,161	0.13
Component 3: non-European ancestry	0.77	0.044	0.021	0.038	10,103	0.70
Trans-ancestry meta-analysis	0.71	0.024	0.004	$1.2x10^{-8}$	148,264	0.42

Locus: *HMGA1*. Lead SNP: rs7742369. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.17	0.027	0.007	0.0011	69,259	0.90
Component 2: UKBB	0.18	0.030	0.007	$2.4x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.18	0.028	0.005	$1.0x10^{-8}$	137,045	0.77
Component 3: non-European ancestry	0.44	0.013	0.016	0.41	9,561	0.18
Trans-ancestry meta-analysis	0.19	0.027	0.005	$1.1x10^{-8}$	146,606	0.16

Locus: *L3MBTL3*. Lead SNP: rs1415701. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.75	0.025	0.006	$2.3x10^{-5}$	75,880	0.69
Component 2: UKBB	0.73	0.025	0.006	$3.2x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.74	0.025	0.004	$2.6x10^{-9}$	143,666	1.00
Component 3: non-European ancestry	0.63	0.048	0.015	0.0013	10,102	0.64
Trans-ancestry meta-analysis	0.73	0.027	0.004	$4.0x10^{-11}$	153,768	0.40

Locus: *ESR1*. Lead SNP: rs1101081. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.72	0.044	0.006	$5.4x10^{-14}$	71,641	0.95
Component 2: UKBB	0.73	0.031	0.006	$2.7x10^{-7}$	67,786	N/A
European ancestry meta-analysis	0.72	0.038	0.004	$1.6x10^{-19}$	139,427	0.14
Component 3: non-European ancestry	0.79	0.027	0.017	0.13	10,103	0.47
Trans-ancestry meta-analysis	0.73	0.037	0.004	$6.1x10^{-20}$	149,530	0.28

Locus: *GNA12*. Lead SNP: rs798489. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.73	0.020	0.006	0.00040	75,884	0.75
Component 2: UKBB	0.73	0.027	0.006	$1.0x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.73	0.023	0.004	$2.0x10^{-8}$	143,670	0.44
Component 3: non-European ancestry	0.92	0.053	0.027	0.048	9,708	0.14
Trans-ancestry meta-analysis	0.74	0.024	0.004	$5.0x10^{-9}$	153,378	0.84

Locus: *IGF2BP3*. Lead SNP: rs11765649. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.76	0.021	0.006	0.00049	71,642	0.80
Component 2: UKBB	0.74	0.032	0.006	$1.3x10^{-7}$	67,786	N/A
European ancestry meta-analysis	0.75	0.027	0.004	$5.8x10^{-10}$	139,428	0.19
Component 3: non-European ancestry	0.87	0.003	0.022	0.88	10,103	0.37
Trans-ancestry meta-analysis	0.76	0.026	0.004	$1.0x10^{-9}$	149,531	0.60

Locus: *TBX20*. Lead SNP: rs6959887. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.61	0.031	0.005	$1.4x10^{-9}$	75,873	0.58
Component 2: UKBB	0.61	0.013	0.006	0.021	67,786	N/A
European ancestry meta-analysis	0.61	0.023	0.004	$1.5x10^{-9}$	143,659	0.013
Component 3: non-European ancestry	0.63	-0.007	0.014	0.65	10,098	0.62
Trans-ancestry meta-analysis	0.61	0.021	0.004	$1.0x10^{-8}$	153,757	0.054

Locus: *YKT6-GCK*. Lead SNP: rs138715366. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.9908	0.227	0.034	$1.7x10^{-11}$	64,557	0.86
Component 2: UKBB	0.9915	0.253	0.031	$7.1x10^{-16}$	67,786	N/A
European ancestry meta-analysis	0.9911	0.241	0.023	$7.2x10^{-26}$	132,343	0.57
Component 3: non-European ancestry	0.9977	0.855	0.333	0.010	3,292	1.00
Trans-ancestry meta-analysis	0.9913	0.244	0.023	$1.4x10^{-26}$	135,635	0.16

Locus: *MLXIPL*. Lead SNP: rs62466330. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.06	0.052	0.011	$1.9x10^{-6}$	74,414	0.24
Component 2: UKBB	0.07	0.046	0.011	$1.5x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.07	0.049	0.008	$1.2x10^{-10}$	142,200	0.70
Component 3: non-European ancestry	0.04	0.142	0.045	0.0015	7,815	0.52
Trans-ancestry meta-analysis	0.07	0.051	0.007	$5.9x10^{-12}$	150,015	0.23

Locus: *ANK1-NKX6-3*. Lead SNP: rs13266210. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.78	0.023	0.006	0.00034	71,643	0.19
Component 2: UKBB	0.79	0.040	0.007	$1.5x10^{-9}$	67,786	N/A
European ancestry meta-analysis	0.79	0.031	0.005	$1.3x10^{-11}$	139,429	0.054
Component 3: non-European ancestry	0.81	0.013	0.019	0.48	9,562	0.30
Trans-ancestry meta-analysis	0.79	0.030	0.004	$1.6x10^{-11}$	148,991	0.32

Locus: *TRIB1*. Lead SNP: rs6989280. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.73	0.026	0.006	$5.6x10^{-6}$	75,885	0.34
Component 2: UKBB	0.73	0.017	0.006	0.0069	67,786	N/A
European ancestry meta-analysis	0.73	0.022	0.004	$2.2x10^{-7}$	143,671	0.25
Component 3: non-European ancestry	0.32	0.027	0.016	0.085	10,104	0.85
Trans-ancestry meta-analysis	0.70	0.022	0.004	$5.0x10^{-8}$	153,775	0.92

Locus: *SLC45A4*. Lead SNP: rs12543725. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.59	0.023	0.005	$1.1x10^{-5}$	71,645	0.39
Component 2: UKBB	0.59	0.023	0.005	$3.0x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.59	0.023	0.004	$1.2x10^{-9}$	139,431	0.94
Component 3: non-European ancestry	0.78	0.005	0.018	0.78	8,653	0.42
Trans-ancestry meta-analysis	0.60	0.022	0.004	$1.9x10^{-9}$	148,084	0.65

Locus: *PTCH1*. Lead SNP: rs28510415. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.09	0.041	0.009	$1.4x10^{-5}$	66,960	0.40
Component 2: UKBB	0.10	0.070	0.009	$1.7x10^{-14}$	67,786	N/A
European ancestry meta-analysis	0.09	0.056	0.007	$1.5x10^{-17}$	134,746	0.023
Component 3: non-European ancestry	0.03	-0.086	0.043	0.049	8,654	0.79
Trans-ancestry meta-analysis	0.09	0.053	0.006	$4.0x10^{-16}$	143,400	0.0055

Locus: *LPAR1*. Lead SNP: rs2150052. Effect/other alleles: T/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.50	0.021	0.005	$8.6x10^{-5}$	71,638	0.23
Component 2: UKBB	0.51	0.021	0.005	$7.5x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.50	0.021	0.004	$2.2x10^{-8}$	139,424	0.95
Component 3: non-European ancestry	0.46	0.008	0.015	0.61	8,655	0.71
Trans-ancestry meta-analysis	0.50	0.020	0.004	$2.8x10^{-8}$	148,079	0.99

Locus: *PHF19*. Lead SNP: rs7847628. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.68	0.028	0.006	$1.1x10^{-6}$	71,638	0.47
Component 2: UKBB	0.68	0.018	0.006	0.0014	67,786	N/A
European ancestry meta-analysis	0.68	0.023	0.004	$1.0x10^{-8}$	139,424	0.23
Component 3: non-European ancestry	0.57	0.017	0.015	0.25	10,104	0.30
Trans-ancestry meta-analysis	0.67	0.023	0.004	$5.4x10^{-9}$	149,528	0.17

Locus: *STRBP*. Lead SNP: rs700059. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.15	0.027	0.007	0.00028	71,641	0.090
Component 2: UKBB	0.14	0.040	0.008	$2.1x10^{-7}$	67,786	N/A
European ancestry meta-analysis	0.14	0.033	0.005	$4.7x10^{-10}$	139,427	0.22
Component 3: non-European ancestry	0.43	0.059	0.016	0.00018	8,653	0.34
Trans-ancestry meta-analysis	0.16	0.036	0.005	$1.2x10^{-12}$	148,080	0.21

Locus: *HHEX-IDE*. Lead SNP: rs61862780. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.51	0.027	0.005	$9.2x10^{-8}$	75,884	0.37
Component 2: UKBB	0.51	0.029	0.005	$7.6x10^{-8}$	67,786	N/A
European ancestry meta-analysis	0.51	0.028	0.004	$3.0x10^{-14}$	143,670	0.81
Component 3: non-European ancestry	0.77	0.025	0.017	0.13	10,103	0.12
Trans-ancestry meta-analysis	0.52	0.028	0.004	$9.5x10^{-15}$	153,773	0.80

Locus: *NT5C2*. Lead SNP: rs74233809. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.08	0.032	0.009	0.00039	75,881	0.88
Component 2: UKBB	0.08	0.042	0.010	$3.0x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.08	0.037	0.007	$5.2x10^{-8}$	143,667	0.49
Component 3: non-European ancestry	0.12	0.061	0.022	0.0057	10,104	0.39
Trans-ancestry meta-analysis	0.08	0.039	0.006	$1.8x10^{-9}$	153,771	0.14

Locus: *ADRB1*. Lead SNP: rs7076938. Effect/other alleles: T/C.

Analysis	EAF	B	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.73	0.046	0.006	$1.3x10^{-15}$	75,885	0.79
Component 2: UKBB	0.73	0.025	0.006	$4.5x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.73	0.036	0.004	$4.7x10^{-18}$	143,671	0.011
Component 3: non-European ancestry	0.64	0.018	0.015	0.22	10,103	0.56
Trans-ancestry meta-analysis	0.73	0.035	0.004	$4.7x10^{-18}$	153,774	0.19

Locus: *PLEKHA1*. Lead SNP: rs2421016. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.50	0.022	0.005	$1.0x10^{-5}$	75,873	0.25
Component 2: UKBB	0.47	0.019	0.005	0.00047	67,786	N/A
European ancestry meta-analysis	0.49	0.021	0.004	$1.8x10^{-8}$	143,659	0.62
Component 3: non-European ancestry	0.40	0.021	0.014	0.15	10,100	0.28
Trans-ancestry meta-analysis	0.48	0.021	0.004	$6.1x10^{-9}$	153,759	0.83

Locus: *INS-IGF2*. Lead SNP: rs72851023. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.07	0.055	0.011	$6.7x10^{-7}$	67,990	0.014
Component 2: UKBB	0.08	0.041	0.010	$8.0x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.07	0.048	0.008	$2.9x10^{-10}$	135,776	0.35
Component 3: non-European ancestry	0.02	-0.048	0.064	0.45	7,815	1.00
Trans-ancestry meta-analysis	0.07	0.046	0.007	$6.8x10^{-10}$	143,591	0.64

Locus: *MTNR1B*. Lead SNP: rs10830963. Effect/other alleles: G/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.28	0.029	0.006	$5.1x10^{-7}$	75,877	0.20
Component 2: UKBB	0.28	0.017	0.006	0.0059	67,786	N/A
European ancestry meta-analysis	0.28	0.023	0.004	$2.9x10^{-8}$	143,663	0.12
Component 3: non-European ancestry	0.20	-0.013	0.021	0.54	10,102	0.76
Trans-ancestry meta-analysis	0.27	0.022	0.004	$1.0x10^{-7}$	153,765	0.23

Locus: *APOLD1*. Lead SNP: rs11055034. Effect/other alleles: C/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.74	0.028	0.006	$2.1x10^{-6}$	75,867	0.91
Component 2: UKBB	0.72	0.016	0.006	0.0099	67,786	N/A
European ancestry meta-analysis	0.73	0.022	0.004	$1.8x10^{-7}$	143,653	0.13
Component 3: non-European ancestry	0.81	0.046	0.020	0.019	9,942	0.67
Trans-ancestry meta-analysis	0.73	0.023	0.004	$2.3x10^{-8}$	153,595	0.32

Locus: *ABCC9*. Lead SNP: rs139975827. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.61	0.027	0.007	$4.9x10^{-5}$	55,417	0.72
Component 2: UKBB	0.63	0.023	0.006	$5.8x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.62	0.025	0.004	$1.1x10^{-8}$	123,203	0.72
Component 3: non-European ancestry	0.70	-0.018	0.018	0.32	8,655	0.68
Trans-ancestry meta-analysis	0.63	0.022	0.004	$1.0x10^{-7}$	131,858	0.22

Locus: *ITPR2*. Lead SNP: rs12823128. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.54	0.017	0.005	0.00086	71,645	0.59
Component 2: UKBB	0.53	0.025	0.005	$3.8x10^{-6}$	67,786	N/A
European ancestry meta-analysis	0.54	0.021	0.004	$1.9x10^{-8}$	139,431	0.32
Component 3: non-European ancestry	0.86	0.000	0.021	1.0	10,103	0.054
Trans-ancestry meta-analysis	0.56	0.020	0.004	$3.2x10^{-8}$	149,534	0.65

Locus: *HMGA2*. Lead SNP: rs1351394. Effect/other alleles: T/C.

Analysis	EAF	B	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.50	0.048	0.005	$7.6x10^{-21}$	75,885	0.40
Component 2: UKBB	0.49	0.039	0.005	$3.1x10^{-13}$	67,786	N/A
European ancestry meta-analysis	0.49	0.044	0.004	$1.9x10^{-32}$	143,671	0.24
Component 3: non-European ancestry	0.34	0.033	0.015	0.028	10,102	0.75
Trans-ancestry meta-analysis	0.48	0.043	0.004	$2.0x10^{-33}$	153,773	0.72

Locus: *IGF1*. Lead SNP: rs7964361. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.08	0.038	0.009	$5.6x10^{-5}$	71,642	0.63
Component 2: UKBB	0.09	0.040	0.010	$2.3x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.09	0.039	0.007	$4.7x10^{-9}$	139,428	0.86
Component 3: non-European ancestry	0.03	-0.010	0.040	0.81	9,264	0.21
Trans-ancestry meta-analysis	0.08	0.038	0.007	$9.7x10^{-9}$	148,692	0.20

Locus: *LINC00332*. Lead SNP: rs2324499. Effect/other alleles: G/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.68	0.026	0.006	$7.9x10^{-6}$	71,639	0.25
Component 2: UKBB	0.67	0.018	0.006	0.0019	67,786	N/A
European ancestry meta-analysis	0.68	0.022	0.004	$7.3x10^{-8}$	139,425	0.34
Component 3: non-European ancestry	0.60	0.034	0.016	0.027	8,655	0.41
Trans-ancestry meta-analysis	0.67	0.023	0.004	$8.3x10^{-9}$	148,080	0.64

Locus: *RB1*. Lead SNP: rs2854355. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.28	0.024	0.006	0.00012	69,775	0.036
Component 2: UKBB	0.26	0.023	0.006	0.00024	67,786	N/A
European ancestry meta-analysis	0.27	0.023	0.004	$9.8x10^{-8}$	137,561	0.91
Component 3: non-European ancestry	0.19	0.037	0.020	0.066	8,654	0.86
Trans-ancestry meta-analysis	0.26	0.024	0.004	$2.2x10^{-8}$	146,215	0.63

Locus: *RNF219-AS1*. Lead SNP: rs1819436. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.86	0.041	0.008	$2.4x10^{-7}$	71,193	0.19
Component 2: UKBB	0.88	0.024	0.008	0.0030	67,786	N/A
European ancestry meta-analysis	0.87	0.033	0.006	$6.3x10^{-9}$	138,979	0.14
Component 3: non-European ancestry	0.84	0.033	0.021	0.12	8,654	0.96
Trans-ancestry meta-analysis	0.87	0.033	0.005	$1.8x10^{-9}$	147,633	0.80

Locus: *FES*. Lead SNP: rs12906125. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.69	0.020	0.006	0.00036	73,495	0.92
Component 2: UKBB	0.67	0.025	0.006	$1.1x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.68	0.023	0.004	$1.7x10^{-8}$	141,281	0.55
Component 3: non-European ancestry	0.75	0.018	0.017	0.30	10,103	0.87
Trans-ancestry meta-analysis	0.69	0.023	0.004	$1.0x10^{-8}$	151,384	0.75

Locus: *IGF1R*. Lead SNP: rs7402982. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.43	0.022	0.005	$4.9x10^{-5}$	71,637	0.24
Component 2: UKBB	0.41	0.024	0.006	$1.3x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.43	0.023	0.004	$2.3x10^{-9}$	139,423	0.83
Component 3: non-European ancestry	0.35	0.020	0.017	0.23	10,103	0.61
Trans-ancestry meta-analysis	0.42	0.023	0.004	$1.1x10^{-9}$	149,526	0.61

Locus: *GPR139*. Lead SNP: rs1011939. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.31	0.022	0.006	0.00013	75,818	0.93
Component 2: UKBB	0.28	0.022	0.006	0.00030	67,786	N/A
European ancestry meta-analysis	0.30	0.022	0.004	$1.3x10^{-7}$	143,604	0.97
Component 3: non-European ancestry	0.57	0.047	0.015	0.0013	10,098	0.52
Trans-ancestry meta-analysis	0.31	0.024	0.004	$2.7x10^{-9}$	153,702	0.66

Locus: *CLDN7*. Lead SNP: rs113086489. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.57	0.033	0.005	$7.1x10^{-10}$	71,640	0.10
Component 2: UKBB	0.55	0.028	0.005	$2.6x10^{-7}$	67,786	N/A
European ancestry meta-analysis	0.56	0.031	0.004	$9.1x10^{-16}$	139,426	0.51
Component 3: non-European ancestry	0.40	0.012	0.015	0.40	10,104	0.29
Trans-ancestry meta-analysis	0.55	0.030	0.004	$1.3x10^{-15}$	149,530	0.77

Locus: *SUZ12P1-CRLF3*. Lead SNP: rs144843919. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.97	0.036	0.018	0.0048	53,571	0.13
Component 2: UKBB	0.96	0.087	0.015	$1.0x10^{-8}$	67,786	N/A
European ancestry meta-analysis	0.96	0.066	0.012	$1.4x10^{-8}$	121,357	0.033
Component 3: non-European ancestry	0.96	0.112	0.049	0.022	6,635	0.056
Trans-ancestry meta-analysis	0.96	0.068	0.011	$1.5x10^{-9}$	127,992	0.068

Locus: *SP6-SP2*. Lead SNP: rs12942207. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.31	0.025	0.006	$2.2x10^{-5}$	71,635	0.85
Component 2: UKBB	0.30	0.020	0.006	0.00063	67,786	N/A
European ancestry meta-analysis	0.30	0.022	0.004	$5.1x10^{-8}$	139,421	0.59
Component 3: non-European ancestry	0.26	0.050	0.018	0.0053	8,654	0.98
Trans-ancestry meta-analysis	0.30	0.024	0.004	$3.0x10^{-9}$	148,075	0.75

Locus: *ACTL9*. Lead SNP: rs61154119. Effect/other alleles: T/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.84	0.030	0.007	$6.4x10^{-5}$	63,412	0.00014
Component 2: UKBB	0.85	0.026	0.007	0.00050	67,786	N/A
European ancestry meta-analysis	0.84	0.028	0.005	$1.1x10^{-7}$	131,198	0.70
Component 3: non-European ancestry	0.79	0.033	0.018	0.077	8,655	0.64
Trans-ancestry meta-analysis	0.84	0.028	0.005	$2.3x10^{-8}$	139,853	0.98

Locus: *PEPD*. Lead SNP: rs10402712. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.25	0.021	0.006	0.00033	71,642	0.23
Component 2: UKBB	0.26	0.022	0.006	0.00042	67,786	N/A
European ancestry meta-analysis	0.26	0.022	0.004	$4.4x10^{-7}$	139,428	0.98
Component 3: non-European ancestry	0.40	0.038	0.014	0.0086	10,102	0.89
Trans-ancestry meta-analysis	0.27	0.023	0.004	$2.3x10^{-8}$	149,530	0.72

Locus: *JAG1*. Lead SNP: rs6040076. Effect/other alleles: C/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.48	0.023	0.005	$3.1x10^{-5}$	71,638	0.82
Component 2: UKBB	0.51	0.023	0.005	$1.8x10^{-5}$	67,786	N/A
European ancestry meta-analysis	0.49	0.023	0.004	$2.0x10^{-9}$	139,424	0.96
Component 3: non-European ancestry	0.69	-0.006	0.018	0.73	8,655	0.026
Trans-ancestry meta-analysis	0.51	0.022	0.004	$7.2x10^{-9}$	148,079	0.24

Locus: *C20orf203*. Lead SNP: rs28530618. Effect/other alleles: A/G.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.50	0.032	0.005	$5.0x10^{-9}$	70,376	0.45
Component 2: UKBB	0.47	0.020	0.005	0.00015	67,786	N/A
European ancestry meta-analysis	0.49	0.026	0.004	$7.7x10^{-12}$	138,162	0.14
Component 3: non-European ancestry	0.63	-0.011	0.016	0.50	10,102	0.25
Trans-ancestry meta-analysis	0.50	0.024	0.004	$8.4x10^{-11}$	148,264	0.18

Locus: *MAFB*. Lead SNP: rs6016377. Effect/other alleles: T/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.41	0.028	0.005	3.8×10^{-7}	71,639	0.10
Component 2: UKBB	0.45	0.020	0.006	0.00043	67,786	N/A
European ancestry meta-analysis	0.43	0.024	0.004	9.5×10^{-10}	139,425	0.29
Component 3: non-European ancestry	0.74	0.025	0.018	0.17	10,103	0.26
Trans-ancestry meta-analysis	0.45	0.024	0.004	3.7×10^{-10}	149,528	0.27

Locus: *NRIP1*. Lead SNP: rs2229742. Effect/other alleles: G/C.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.85	0.037	0.008	6.6×10^{-6}	75,886	0.66
Component 2: UKBB	0.90	0.034	0.009	9.1×10^{-5}	67,786	N/A
European ancestry meta-analysis	0.87	0.036	0.006	2.2×10^{-9}	143,672	0.82
Component 3: non-European ancestry	0.82	-0.085	0.044	0.052	9,264	0.72
Trans-ancestry meta-analysis	0.87	0.034	0.006	1.5×10^{-8}	152,936	0.092

Locus: *KREMEN1*. Lead SNP: rs134594. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.35	0.022	0.006	8.9×10^{-5}	69,554	0.36
Component 2: UKBB	0.35	0.023	0.006	3.2×10^{-5}	67,786	N/A
European ancestry meta-analysis	0.35	0.023	0.004	1.0×10^{-8}	137,340	0.84
Component 3: non-European ancestry	0.33	0.002	0.016	0.90	8,655	0.59
Trans-ancestry meta-analysis	0.35	0.022	0.004	2.2×10^{-8}	145,995	0.25

Locus: *SREBF2*. Lead SNP: rs62240962. Effect/other alleles: C/T.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.91	0.054	0.010	2.6×10^{-8}	68,286	0.69
Component 2: UKBB	0.92	0.040	0.010	6.0×10^{-5}	67,786	N/A
European ancestry meta-analysis	0.91	0.047	0.007	9.7×10^{-12}	136,072	0.30
Component 3: non-European ancestry	0.97	0.07	0.048	0.15	7,815	0.028
Trans-ancestry meta-analysis	0.92	0.047	0.007	3.7×10^{-12}	143,887	0.69

Locus: *PLAC1*. Lead SNP: rs11096402. Effect/other alleles: G/A.

Analysis	EAF	β	SE	*P*-value	*N*	*Q P*-value
Component 1: European ancestry	0.28	0.027	0.007	2.0×10^{-4}	37,417	0.73
Component 2: UKBB	0.24	0.028	0.006	1.8×10^{-6}	57,620	N/A
European ancestry meta-analysis	0.25	0.028	0.005	1.3×10^{-9}	95,037	0.31
Component 3: non-European ancestry	N/A	N/A	N/A	N/A	N/A	N/A
Trans-ancestry meta-analysis	N/A	N/A	N/A	N/A	N/A	N/A

PLAC1 result (on X chromosome) was not available in non-European ancestry studies.
EAF, effect allele frequency; SE, standard error.

Supplementary Table 4. Summary statistics for lead SNPs attaining genome-wide significant evidence ($P<5x10^{-8}$) of association with BW in European ancestry meta-analysis of up to 143,677 individuals and/or trans-ancestry meta-analysis of up to 153,781 individuals.

Locus	SNP	Chr	Position (b37, bp)	Alleles		EAF	European ancestry		Trans-ancestry		Status[a]	EUR r^2 with lead TA	Present in HapMap?	Best proxy in HapMap	
				Effect	Other		β (SE)	*P*-value	β (SE)	*P*-value				SNP	EUR r^2
WNT4-ZBTB40	rs2473248	1	22,536,643	C	T	0.87	0.033 (0.006)	$1.1x10^{-8}$	0.033 (0.005)	$1.1x10^{-9}$	TA/EUR		No	rs2744726	0.99
ZBTB7B	rs3753639	1	154,986,091	C	T	0.24	0.031 (0.004)	$7.3x10^{-12}$	0.031 (0.004)	$1.3x10^{-12}$	TA/EUR		No	rs905938	0.77
FCGR2B	rs72480273	1	161,644,871	C	A	0.17	0.031 (0.005)	$8.0x10^{-10}$	0.030 (0.005)	$1.5x10^{-9}$	TA/EUR		No	rs17413015	0.97
DTL	rs61830764	1	212,289,976	A	G	0.38	0.022 (0.004)	$5.6x10^{-8}$	0.022 (0.004)	$4.5x10^{-8}$	TA		No	rs1387815	0.51
ATAD2B	rs7575873	2	23,962,647	A	G	0.88	0.038 (0.006)	$1.3x10^{-11}$	0.036 (0.006)	$6.2x10^{-11}$	TA		No	rs718139	0.98
	rs181211713	2	23,965,445	G	A	0.87	0.038 (0.006)	$1.2x10^{-11}$	0.036 (0.005)	$7.3x10^{-11}$	EUR	0.94	No		
EPAS1	rs1374204	2	46,484,205	T	C	0.70	0.047 (0.004)	$6.2x10^{-29}$	0.046 (0.004)	$1.5x10^{-29}$	TA		Yes		
	rs17034876	2	46,484,310	T	C	0.70	0.047 (0.004)	$2.6x10^{-29}$	0.046 (0.004)	$1.9x10^{-29}$	EUR	0.99	Yes		
PTH1R	rs2242116	3	46,941,116	A	G	0.38	0.022 (0.004)	$1.4x10^{-8}$	0.021 (0.004)	$1.2x10^{-8}$	TA		Yes		
	rs2168443	3	46,947,087	T	A	0.38	0.023 (0.004)	$3.5x10^{-9}$	0.021 (0.004)	$1.3x10^{-8}$	EUR	0.99	Yes		
ADCY5	rs11719201	3	123,068,744	T	C	0.23	0.046 (0.004)	$2.4x10^{-26}$	0.046 (0.004)	$6.4x10^{-27}$	TA/EUR		No	rs7613951	0.97
	rs9883204	3	123,096,820	T	C	0.25	0.041 (0.004)	$8.4x10^{-22}$	0.040 (0.004)	$6.1x10^{-22}$	Previous	0.85	Yes		
CPA3	rs10935733	3	148,622,968	T	C	0.41	0.022 (0.004)	$9.2x10^{-9}$	0.023 (0.004)	$6.2x10^{-10}$	TA/EUR		No	rs12496367	0.81
CCNL1-LEKR1	rs13322435	3	156,795,468	A	G	0.60	0.053 (0.004)	$3.7x10^{-41}$	0.052 (0.004)	$1.3x10^{-42}$	TA		Yes		
	rs900399	3	156,798,732	A	G	0.61	0.052 (0.004)	$2.2x10^{-41}$	0.051 (0.004)	$2.9x10^{-41}$	EUR	0.92	Yes		
	rs900400	3	156,798,775	T	C	0.61	0.053 (0.004)	$1.1x10^{-40}$	0.051 (0.004)	$8.4x10^{-41}$	Previous	0.92	Yes		
LCORL	rs925098	4	17,919,811	G	A	0.27	0.034 (0.004)	$5.4x10^{-16}$	0.032 (0.004)	$1.3x10^{-15}$	TA		Yes		
	rs2724475	4	17,946,432	T	C	0.27	0.034 (0.004)	$5.3x10^{-16}$	0.032 (0.004)	$1.3x10^{-15}$	EUR	0.97	Yes		
	rs724577	4	17,993,410	A	C	0.27	0.033 (0.004)	$1.7x10^{-15}$	0.031 (0.004)	$1.5x10^{-14}$	Previous	0.98	Yes		

Locus	SNP	Chr	Position (b37, bp)	Alleles		EAF	European ancestry		Trans-ancestry		Status[a]	EUR r^2 with lead TA	Present in HapMap?	Best proxy in HapMap	
				Effect	Other		β (SE)	*P*-value	β (SE)	*P*-value				SNP	EUR r^2
HHIP	rs6537307	4	145,601,863	G	A	0.50	0.025 (0.004)	$9.5x10^{-12}$	0.026 (0.004)	$1.3x10^{-12}$	TA		Yes		
	rs2131354	4	145,599,908	A	G	0.53	0.026 (0.004)	$4.1x10^{-12}$	0.026 (0.004)	$2.3x10^{-12}$	EUR	0.88	No		
5q11.2	rs854037	5	57,091,783	A	G	0.81	0.027 (0.005)	$2.2x10^{-8}$	0.025 (0.005)	$3.5x10^{-8}$	TA/EUR		Yes		
	rs4432842	5	57,172,078	T	C	0.70	0.021 (0.004)	$3.4x10^{-7}$	0.019 (0.004)	$7.0x10^{-7}$	Previous	0.47	Yes		
EBF1	rs7729301	5	157,886,953	A	G	0.73	0.024 (0.004)	$1.6x10^{-8}$	0.025 (0.004)	$1.3x10^{-9}$	TA		No	rs2946164	0.97
	rs2946179	5	157,886,627	C	T	0.73	0.024 (0.004)	$1.3x10^{-8}$	0.024 (0.004)	$1.5x10^{-9}$	EUR	0.98	No		
CDKAL1	rs35261542	6	20,675,792	C	A	0.73	0.044 (0.004)	$4.4x10^{-27}$	0.044 (0.004)	$9.7x10^{-29}$	TA/EUR		No	rs7756992	0.97
	rs6931514	6	20,703,952	A	G	0.73	0.043 (0.004)	$6.2x10^{-26}$	0.043 (0.004)	$1.0x10^{-26}$	Previous	0.94	Yes		
HIST1H2BE	rs9379832	6	26,186,200	A	G	0.70	0.023 (0.004)	$6.6x10^{-8}$	0.024 (0.004)	$1.2x10^{-8}$	TA		No	rs806794	0.62
HMGA1	rs7742369	6	34,165,721	G	A	0.18	0.028 (0.005)	$1.0x10^{-8}$	0.027 (0.005)	$1.1x10^{-8}$	TA		Yes		
	rs1187118	6	34,169,020	A	T	0.17	0.030 (0.005)	$3.6x10^{-9}$	0.027 (0.005)	$1.4x10^{-8}$	EUR	0.95	No		
L3MBTL3	rs1415701	6	130,345,835	G	A	0.74	0.025 (0.004)	$2.6x10^{-9}$	0.027 (0.004)	$4.0x10^{-11}$	TA/EUR		Yes		
ESR1	rs1101081	6	152,032,917	C	T	0.72	0.038 (0.004)	$1.6x10^{-19}$	0.037 (0.004)	$6.1x10^{-20}$	TA		No	rs851977	0.99
	rs10872678	6	152,039,964	T	C	0.72	0.038 (0.004)	$6.9x10^{-20}$	0.036 (0.004)	$1.3x10^{-19}$	EUR	0.98	Yes		
GNA12	rs798489	7	2,801,803	C	T	0.73	0.023 (0.004)	$2.0x10^{-8}$	0.024 (0.004)	$5.0x10^{-9}$	TA		Yes		
	rs798498	7	2,795,882	T	G	0.69	0.023 (0.004)	$1.3x10^{-8}$	0.022 (0.004)	$3.8x10^{-8}$	EUR	0.83	Yes		
IGF2BP3	rs11765649	7	23,479,013	T	C	0.75	0.027 (0.004)	$5.8x10^{-10}$	0.026 (0.004)	$1.0x10^{-9}$	TA/EUR		No	rs12540730	0.86
TBX20	rs6959887	7	35,295,365	A	G	0.61	0.023 (0.004)	$1.5x10^{-9}$	0.021 (0.004)	$1.0x10^{-8}$	TA/EUR		Yes		
YKT6-GCK	rs138715366	7	44,246,271	C	T	0.99	0.241 (0.023)	$7.2x10^{-26}$	0.244 (0.023)	$1.4x10^{-26}$	TA/EUR		No	rs2908277	0.096
MLXIPL	rs62466330	7	73,056,805	C	T	0.07	0.049 (0.008)	$1.2x10^{-10}$	0.051 (0.007)	$5.9x10^{-12}$	TA		No	rs17401675	1
	rs111778406	7	72,957,570	G	A	0.07	0.049 (0.008)	$5.8x10^{-11}$	0.050 (0.007)	$1.3x10^{-11}$	EUR	0.78	No		

Locus	SNP	Chr	Position	Alleles		EAF	European ancestry		Trans-ancestry		Status[a]	EUR r^2 with lead TA	Present in HapMap?	Best proxy in HapMap	
			(b37, bp)	Effect	Other		β (SE)	*P*-value	β (SE)	*P*-value				SNP	EUR r^2
ANK1-NKX6.3	rs13266210	8	41,533,514	A	G	0.79	0.031 (0.005)	$1.3x10^{-11}$	0.030 (0.004)	$1.6x10^{-11}$	TA/EUR		Yes		
TRIB1	rs6989280	8	126,508,746	G	A	0.73	0.022 (0.004)	$2.2x10^{-7}$	0.022 (0.004)	$5.0x10^{-8}$	TA		Yes		
SLC45A4	rs12543725	8	142,247,979	G	A	0.59	0.023 (0.004)	$1.2x10^{-9}$	0.022 (0.004)	$1.9x10^{-9}$	TA/EUR		Yes		
PTCH1	rs28510415	9	98,245,026	G	A	0.09	0.056 (0.007)	$1.5x10^{-17}$	0.053 (0.006)	$4.0x10^{-16}$	TA		No	rs3824488	1
	rs3780573	9	98,239,503	A	G	0.10	0.055 (0.006)	$7.0x10^{-18}$	0.050 (0.006)	$1.1x10^{-15}$	EUR	1.00	No		
LPAR1	rs2150052	9	113,945,067	T	A	0.50	0.021 (0.004)	$2.2x10^{-8}$	0.020 (0.004)	$2.8x10^{-8}$	TA		Yes		
	rs1411424	9	113,892,963	A	G	0.52	0.021 (0.004)	$2.2x10^{-8}$	0.020 (0.004)	$4.1x10^{-8}$	EUR	0.86	Yes		
PHF19	rs7847628	9	123,631,225	G	A	0.68	0.023 (0.004)	$1.0x10^{-8}$	0.023 (0.004)	$5.4x10^{-9}$	TA		Yes	rs1056567	0.87
	rs4836833	9	123,632,829	C	G	0.67	0.023 (0.004)	$8.6x10^{-9}$	0.022 (0.004)	$1.5x10^{-8}$	EUR	0.88	Yes		
STRBP	rs700059	9	125,824,055	G	A	0.14	0.033 (0.005)	$4.7x10^{-10}$	0.036 (0.005)	$1.2x10^{-12}$	TA		Yes		
	rs10818797	9	126,020,405	C	T	0.14	0.035 (0.005)	$1.2x10^{-10}$	0.035 (0.005)	$1.5x10^{-11}$	EUR	0.91	Yes		
HHEX-IDE	rs61862780	10	94,468,643	T	C	0.51	0.028 (0.004)	$3.0x10^{-14}$	0.028 (0.004)	$9.5x10^{-15}$	TA		No	rs2497306	0.97
	rs2497304	10	94,492,716	C	T	0.52	0.028 (0.004)	$2.6x10^{-14}$	0.028 (0.004)	$1.4x10^{-14}$	EUR	0.90	Yes		
NT5C2	rs74233809	10	104,913,940	C	T	0.08	0.037 (0.007)	$5.2x10^{-8}$	0.039 (0.006)	$1.8x10^{-9}$	TA		No	rs11191582	1
	rs79237883	10	104,940,946	C	T	0.08	0.037 (0.007)	$3.6x10^{-8}$	0.038 (0.006)	$5.6x10^{-9}$	EUR	1.00	No		
ADRB1	rs7076938	10	115,789,375	T	C	0.73	0.036 (0.004)	$4.7x10^{-18}$	0.035 (0.004)	$4.7x10^{-18}$	TA		Yes		
	rs740746	10	115,792,787	A	G	0.73	0.036 (0.004)	$3.8x10^{-18}$	0.035 (0.004)	$6.4x10^{-18}$	EUR	0.99	Yes		
	rs1801253	10	115,805,056	C	G	0.71	0.032 (0.004)	$3.0x10^{-14}$	0.031 (0.004)	$2.6x10^{-14}$	Previous	0.99	Yes		
PLEKHA1	rs2421016	10	124,167,512	T	C	0.49	0.021 (0.004)	$1.8x10^{-8}$	0.021 (0.004)	$6.1x10^{-9}$	TA/EUR		Yes		
INS-IGF2	rs72851023	11	2,130,620	T	C	0.07	0.048 (0.008)	$2.9x10^{-10}$	0.046 (0.007)	$6.8x10^{-10}$	TA/EUR		No	rs868332	0.49
MTNR1B	rs10830963	11	92,708,710	G	C	0.28	0.023 (0.004)	$2.9x10^{-8}$	0.022 (0.004)	$1.0x10^{-7}$	EUR		Yes		

Locus	SNP	Chr	Position	Alleles		EAF	European ancestry		Trans-ancestry		Status[a]	EUR r^2 with lead TA	Present in HapMap?	Best proxy in HapMap	
			(b37, bp)	Effect	Other		β (SE)	*P*-value	β (SE)	*P*-value				SNP	EUR r^2
APOLD1	rs11055034	12	12,890,626	C	A	0.73	0.022 (0.004)	$1.8x10^{-7}$	0.023 (0.004)	$2.3x10^{-8}$	TA		Yes		
ABCC9	rs139975827	12	22,068,161	G	A	0.62	0.025 (0.004)	$1.1x10^{-8}$	0.022 (0.004)	$1.0x10^{-7}$	EUR		No	rs4148656	0.67
ITPR2	rs12823128	12	26,872,730	T	C	0.54	0.021 (0.004)	$1.9x10^{-8}$	0.020 (0.004)	$3.2x10^{-8}$	TA		Yes		
	rs2306547	12	26,877,885	C	T	0.54	0.021 (0.004)	$1.8x10^{-8}$	0.020 (0.004)	$3.2x10^{-8}$	EUR	0.96	Yes		
HMGA2	rs1351394	12	66,351,826	T	C	0.49	0.044 (0.004)	$1.9x10^{-32}$	0.043 (0.004)	$2.0x10^{-33}$	TA/EUR		Yes		
	rs1042725	12	66,358,347	C	T	0.51	0.043 (0.004)	$3.1x10^{-32}$	0.042 (0.004)	$7.1x10^{-32}$	Previous	0.93	Yes		
IGF1	rs7964361	12	102,994,878	A	G	0.09	0.039 (0.007)	$4.7x10^{-9}$	0.038 (0.007)	$9.7x10^{-9}$	TA/EUR		Yes		
LINC00332	rs2324499	13	40,662,001	G	C	0.68	0.022 (0.004)	$7.3x10^{-8}$	0.023 (0.004)	$8.3x10^{-9}$	TA		Yes		
	rs7998537	13	40,662,742	G	A	0.68	0.022 (0.004)	$3.9x10^{-8}$	0.022 (0.004)	$1.8x10^{-8}$	EUR	1.00	Yes		
RB1	rs2854355	13	48,882,363	G	A	0.27	0.023 (0.004)	$9.8x10^{-8}$	0.024 (0.004)	$2.2x10^{-8}$	TA		No	rs9568028	0.88
	rs34217484	13	48,854,550	A	T	0.26	0.024 (0.004)	$4.8x10^{-8}$	0.023 (0.004)	$5.8x10^{-8}$	EUR	0.85	No		
RNF219-AS1	rs1819436	13	78,580,283	C	T	0.87	0.033 (0.006)	$6.3x10^{-9}$	0.033 (0.005)	$1.8x10^{-9}$	TA/EUR		No	rs944379	0.88
FES	rs12906125	15	91,427,612	G	A	0.68	0.023 (0.004)	$1.7x10^{-8}$	0.023 (0.004)	$1.0x10^{-8}$	TA/EUR		No	rs6227	0.87
IGF1R	rs7402982	15	99,193,269	A	G	0.43	0.023 (0.004)	$2.3x10^{-9}$	0.023 (0.004)	$1.1x10^{-9}$	TA/EUR		No	rs8028620	0.55
GPR139	rs1011939	16	19,992,996	G	A	0.30	0.022 (0.004)	$1.3x10^{-7}$	0.024 (0.004)	$2.7x10^{-9}$	TA		No	rs1858988	0.70
CLDN7	rs113086489	17	7,171,356	T	C	0.56	0.031 (0.004)	$9.1x10^{-16}$	0.030 (0.004)	$1.3x10^{-15}$	TA/EUR		No	rs5417	0.80
SUZ12P1-CRLF3	rs144843919	17	29,037,339	G	A	0.97	0.066 (0.012)	$1.4x10^{-8}$	0.068 (0.011)	$1.5x10^{-9}$	TA/EUR		No	rs8073965	0.22
SP6-SP2	rs12942207	17	45,968,294	C	T	0.30	0.022 (0.004)	$5.1x10^{-8}$	0.024 (0.004)	$3.0x10^{-9}$	TA		No	rs11079800	0.91
	rs72833480	17	45,964,861	A	G	0.29	0.023 (0.004)	$4.6x10^{-8}$	0.023 (0.004)	$2.1x10^{-8}$	EUR	0.94	No		
ACTL9	rs61154119	19	8,787,750	T	G	0.84	0.028 (0.005)	$1.1x10^{-7}$	0.028 (0.005)	$2.3x10^{-8}$	TA		No	rs2967684	1
PEPD	rs10402712	19	33,926,013	A	G	0.26	0.022 (0.004)	$4.4x10^{-7}$	0.023 (0.004)	$2.3x10^{-8}$	TA		No	rs17833935	0.54

Locus	SNP	Chr	Position	Alleles		EAF	European ancestry		Trans-ancestry		Status[a]	EUR r^2 with lead TA	Present in HapMap?	Best proxy in HapMap	
			(b37, bp)	Effect	Other		β (SE)	*P*-value	β (SE)	*P*-value				SNP	EUR r^2
JAG1	rs6040076	20	10,658,882	C	G	0.49	0.023 (0.004)	$2.0x10^{-9}$	0.022 (0.004)	$7.2x10^{-9}$	TA/EUR		No	rs2206815	0.85
C20orf203	rs28530618	20	31,275,581	A	G	0.49	0.026 (0.004)	$7.7x10^{-12}$	0.024 (0.004)	$8.4x10^{-11}$	TA/EUR		No	rs6057610	0.82
MAFB	rs6016377	20	39,172,728	T	C	0.43	0.024 (0.004)	$9.5x10^{-10}$	0.024 (0.004)	$3.7x10^{-10}$	TA/EUR		Yes		
NRIP1	rs2229742	21	16,339,172	G	C	0.87	0.036 (0.006)	$2.2x10^{-9}$	0.034 (0.006)	$1.5x10^{-8}$	TA/EUR		Yes		
KREMEN1	rs134594	22	29,468,456	C	T	0.35	0.023 (0.004)	$1.0x10^{-8}$	0.022 (0.004)	$2.2x10^{-8}$	TA/EUR		Yes		
SREBF2	rs62240962	22	42,259,524	C	T	0.91	0.047 (0.007)	$9.7x10^{-12}$	0.047 (0.007)	$3.7x10^{-12}$	TA/EUR		No	rs10483213	0.70
PLAC1	rs11096402	X	133,827,868	G	A	0.28	0.028 (0.005)	$1.3x10^{-9}$	N/A	N/A	EUR		Yes		

Chr, chromosome; bp, base pair; EAF, effect allele frequency; SE, standard error.

[a]Status indicates whether the SNP was lead in European ancestry (EUR) or trans-ancestry (TA) meta-analysis. Previous denotes previously reported lead SNP[5] at established loci.

Supplementary Table 5. Loci with multiple distinct association signals attaining genome-wide significance ($P<5x10^{-8}$) in approximate conditional meta-analysis of 143,677 individuals of European ancestry, using 5,000 white British participants from UK BioBank as a reference for linkage disequilibrium.

Locus	Index variant	Chr	Position (b37, bp)	Alleles	EAF	Unconditional meta-analysis		Conditional meta-analysis			UKBB reference r^2	Present in HapMap?	Best proxy in HapMap	
				Effect/ Other		β (SE)	*P*-value	Conditioned on	β (SE)	*P*-value			SNP	EUR r^2
ZBTB7B	rs3753639	1	154,986,091	C/T	0.24	0.031 (0.004)	$7.3x10^{-12}$	rs4330912	0.034 (0.005)	$2.2x10^{-14}$	0.019	No	rs905938	0.77
	rs4330912	1	155,969,428	G/C	0.64	0.021 (0.004)	$1.8x10^{-7}$	rs3753639	0.025 (0.004)	$5.4x10^{-10}$		No	rs12043212	0.93
HMGA1	rs9368777	6	33,788,637	C/G	0.58	0.022 (0.004)	$2.2x10^{-8}$	rs1187118	0.021 (0.004)	$3.3x10^{-8}$	0.000	No	rs4304152	0.57
	rs1187118	6	34,169,020	A/T	0.17	0.030 (0.005)	$3.6x10^{-9}$	rs9368777	0.030 (0.005)	$5.4x10^{-9}$		No	rs1776877	0.95
PTCH1	rs12551019	9	96,949,079	C/T	0.68	0.022 (0.004)	$3.1x10^{-8}$	rs3780573	0.024 (0.004)	$5.1x10^{-9}$	0.001	Yes		
	rs3780573	9	98,239,503	A/G	0.10	0.055 (0.006)	$7.0x10^{-18}$	rs12551019	0.057 (0.006)	$1.2x10^{-18}$		No	rs3824488	1.00

Chr, chromosome; bp, base pair; EAF, effect allele frequency; SE, standard error.

Supplementary Table 6. Candidate gene(s) at birth weight loci.

Locus	Lead SNP	Chr	Position (b37)	Candidate gene(s) in the locus[a]	Reports on eQTL[b]	Literature search for nearby genes (300kb)	Coding variants (EUR r^2 with the lead SNP)
WNT4-ZBTB40	rs2473248	1	22,536,643	*WNT4[P,N], CDC42[B]*	*WNT4:* Cerebellum and temporal cortex eQTL; *CDC42:* Whole blood eQTL (proxy SNP)		-
ZBTB7B	rs3753639	1	154,986,091	*SHC1[B], S100A7[P]*		*SHC1*: The Shc adaptor proteins are key transducers of growth promotion and gene expression, and are phosphorylated by all known receptor tyrosine.	-
FCGR2B	rs72480273	1	161,644,871	*ATF6[B], APOA2[P], FCGR2B[N]*	*ATF6:* Cerebellum and temporal cortex eQTL; *FCGR2B:* Whole blood, cerebellum and temporal cortex eQTL	*HSPA6*: higher expression of HSPA6 in placental vascular disease (PVD) vs controls; HSPA6 encodes HSP70 which was found to be upregulated in PVD vs control placenta and microvascular endothelial cells. HSP70 mRNA and protein expression also correlated negatively with infant birth weight (PMID:18372927).	-
DTL	rs61830764	1	212,289,976	*DTL[N]*			-
ATAD2B	rs7575873	2	23,962,647	*ATAD2B[N], FKBP1B[P]*	*PFN4:* Lymphoblastoid eQTL		-
EPAS1	rs1374204	2	46,484,205	*RHOQ[B], SOCS5[P]*	*EPAS1, PRKCE*: Cerebellum and temporal cortex eQTL	*EPAS1*: involved in the hypoxic response and is suggested to be responsible for the genetic adaptation of high-altitude hypoxia in Tibetans. PMID 25501874 found associations of 2 variants with BW in small sample-sized Tibetans.	-
PTH1R	rs2242116	3	46,941,116	*PTH1R[B,N], CCR1[P]*	*CCDC12:* Whole blood, cerebellum and temporal cortex eQTL		-
ADCY5	rs11719201	3	123,068,744	*ADCY5[B,N], HCLS1[P]*	*ADCY5:* Cerebellum and temporal cortex eQTL (proxy SNP)		-
CPA3	rs10935733	3	148,622,968	*AGTR1[B,P]*	*CPA3,CPB1: eQTL* (proxy SNP)	*AGTR1* = angiotensin II receptor gene: good candidate as the protein mediates processes important for placentation. Levels of protein higher in umbilical cord and maternal peripheral blood in preeclampsia than in controls; levels of mRNA higher in placenta of preeclampsia than control pregnancies; birth weight negatively correlated with levels in cord (PMID 23302726).	-
CCNL1-LEKR1	rs13322435	3	156,795,468	*LEKR1[N], IL12A[P]*	*LEKR1:* Temporal cortex eQTL; CCNL1: Whole blood, cerebellum and temporal cortex eQTL		-
LCORL	rs925098	4	17,919,811	*LCORL[N], SLIT2[P]*	*LCORL:* Cerebellum and temporal cortex eQTL	Adipose tissue and muscle expression in cattle of *NCAPG* and *LCORL* associated with feed intake and weight gain in cattle (these are in a QTL for body weight in cattle).	-
HHIP	rs6537307	4	145,601,863	*HHIP[N], ANAPC10[P]*	*HHIP:* Cerebellum and temporal cortex eQTL		-
5q11.2	rs854037	5	57,091,783	*ACTBL2[N], IL6ST[P]*			-
EBF1	rs7729301	5	157,886,953	*EBF1[N,B], FABP6[P]*			-
CDKAL1	rs35261542	6	20,675,792	*CDKAL1[B], SOX4[P]*	*CDKAL1:* Cerebellum and temporal cortex eQTL		-

Locus	Lead SNP	Chr	Position (b37)	Candidate gene(s) in the locus[a]	Reports on eQTL[b]	Literature search for nearby genes (300kb)	Coding variants (EUR r^2 with the lead SNP)
HIST1H2BE	rs9379832	6	26,186,200	*HIST1H2BE[N,B], BTN2A2[P]*			-
HMGA1	rs7742369	6	34,165,721	*HMGA1[N,B], GRM4[B], MAPK14[P]*	*HMGA1:* Cerebellum and temporal cortex eQTL		-
L3MBTL3	rs1415701	6	130,345,835	*L3MBTL3[E,N], SAMD3[E], ENPP1[P]*	*L3MBTL3, SAMD3:* Whole blood, cerebellum and temporal cortex eQTLs		-
ESR1	rs1101081	6	152,032,917	*ESR1[N,B], LATS1[P]*	*ESR1: M*onocyte, cerebellum and temporal cortex eQTL (for proxy SNP)		-
GNA12	rs798489	7	2,801,803	*GNA12[N,E], PDGFA[N]*	*GNA12:* Nerve tibial, lymphoblastid, whole blood, cerebellum and temporal cortex eQTL		-
IGF2BP3	rs11765649	7	23,479,013	*IGF2BP3[N,B], NPY[P]*	*CCDC126: lymphoblastoid eQTL*		-
TBX20	rs6959887	7	35,295,365	*TBX20[N], SEPT7[P]*	*TBX20:* Cerebellum and temporal cortex eQTL		-
YKT6-GCK	rs138715366	7	44,246,271	*YKT6[N], GCK[B]*		*GCK* mutations reduce birth weight and increase fasting glucose (Hattersley et al 1999, Nat Genet).	-
MLXIPL	rs62466330	7	73,056,805	*MLXIPL[N], FZD9[P]*	*MLXIPL:* Cerebellum and temporal cortex eQTL (for proxy SNP)		-
ANK1-NKX6-3	rs13266210	8	41,533,514	*ANK1[N,B], SFRP1[P]*	*ANK1:* Cerebellum, temporal cortex and lung eQTL		-
TRIB1	rs6989280	8	126,508,746	*TRIB1[N], MYC[P]*	*TRIB1:* Cerebellum and temporal cortex eQTL		-
SLC45A4	rs12543725	8	142,247,979	*SLC45A4[N,E], PTK2[B,P]*	*SLC45A4:* Whole blood, cerebellum and temporal cortex eQTL		-
PTCH1	rs28510415	9	98,245,026	*PTCH1[N,B], FOXE1[P]*	*PTCH1:* Whole blood, cerebellum and temporal cortex eQTL (for proxy SNP)	*FANCC*: mutations result in Fanconi anaemia (associated with low birth weight and shorter stature).	-
LPAR1	rs2150052	9	113,945,067	*LPAR1[N,E,B,P]*	*LPAR1:* whole blood eQTL		-
PHF19	rs7847628	9	123,631,225	*C5[B], DAB2IP[P]*	*C5:* naïve monocyte, whole blood, cerebellum and temporal cortex eQTL		-
STRBP	rs700059	9	125,824,055	*STRBP[E], C5[P]*	*STRBP:* Whole blood, cerebellum and temporal cortex eQTL		-
HHEX-IDE	rs61862780	10	94,468,643	*IDE[B], PLCE1[P]*	*HHEX:* monocyte, whole blood, cerebellum and temporal cortex eQTL		-
NT5C2	rs74233809	10	104,913,940	*NT5C2[N], CHUK[P]*		*CYP17A1*: mutation in maternal *CYP17A1* is associated with small for gestational age (SGA) (PMID 14665706)	-
ADRB1	rs7076938	10	115,789,375	*ADRB1[N,C,B], AFAP1L2[P]*	*ADRB1: cerebellum and temporal cortex eQTL*		rs1801253 (G389R, r^2=0.99, damaging)
PLEKHA1	rs2421016	10	124,167,512	*PLEKHA1[N,E], FGFR2[P]*	*PLEKHA1:* Whole blood, cerebellum and temporal cortex eQTL		-
INS-IGF2	rs72851023	11	2,130,620	*INS-IGF2[N,B,imp]*			-

Locus	Lead SNP	Chr	Position (b37)	Candidate gene(s) in the locus[a]	Reports on eQTL[b]	Literature search for nearby genes (300kb)	Coding variants (EUR r^2 with the lead SNP)
MTNR1B	rs10830963	11	92,708,710	*MTNR1B[N,B,P]*	*MTNR1B:* Cerebellum and temporal cortex eQTL		-
APOLD1	rs11055034	12	12,890,626	*CDKN1B[B,E,P], HEBP1[B]*	*CDKN1B:* Cerebellum and temporal cortex eQTL		-
ABCC9	rs139975827	12	22,068,161	*ABCC9[N], KRAS[P]*			-
ITPR2	rs12823128	12	26,872,730	*ITPR2[N,B]*	*ITPR2:* Cerebellum and temporal cortex eQTL		-
HMGA2	rs1351394	12	66,351,826	*HMGA2[N,B], IRAK3[P]*	*HMGA2:* Cerebellum and temporal cortex eQTL	*HMGA2:* 12q14 microdeletion syndrome implicates *HMGA2* as causal to height (PMID: 17220210 and 19298872).	-
IGF1	rs7964361	12	102,994,878	*IGF1[N,B,P]*			-
LINC00332	rs2324499	13	40,662,001	*LINC00332[N], TNFSF11[P]*			-
RB1	rs2854355	13	48,882,363	*RB1[N,B,P,imp], LPAR6[imp,B]*	*RB1:* Whole blood, cerebellum and temporal cortex eQTL		-
RNF219-AS1	rs1819436	13	78,580,283	*EDNRB[B,P]*	*EDNRB:* Monocyte, cerebellum and temporal cortex eQTL (for proxy SNP)		-
FES	rs12906125	15	91,427,612	*FES[N,E], MESP1[P]*	*FES:* Thyroid, whole blood, cerebellum, temporal cortex and tibial nerve eQTL	*FURIN*: a ubiquitous proprotein convertase, the major processing enzyme of the secretory pathway. It is involved in processing proinsulin to insulin, and in processing proIGF2 (PMID 9660813).	-
IGF1R	rs7402982	15	99,193,269	*IGF1R[B]*			-
GPR139	rs1011939	16	19,992,996	*GPR139[N], RPS15A[P]*			-
CLDN7	rs113086489	17	7,171,356	*SLC2A4[B], POLR2A[S], DVL2[P]*	*SLC2A4:* Cerebellum and temporal cortex eQTL; *DVL2:* monocyte, whole blood, cerebellum and temporal cortex eQTL (for proxy SNP)	*SLC2A4 (GLUT4):* an insulin responsive glucose transporter. PMID 24062248 showed lower mRNA in preadipocytes from LBW vs NBW. Protein level of SLCA24 was lower in adipose tissue of LBW men compared to NMW (PMID 17063325).	-
SUZ12P1-CRLF3	rs144843919	17	29,037,339	*SUZ12P1[N]*			-
SP6-SP2	rs12942207	17	45,968,294	*SP2[N], NGFR[P]*	*SP2:* Whole blood, cerebellum and temporal cortex eQTL (for proxy SNP)		-
ACTL9	rs61154119	19	8,787,750	*ACTL9[N], INSR[P]*			-
PEPD	rs10402712	19	33,926,013	*CEBPA[B]*		*CEBPA:* an adipogenic transcription factor involved in adipocyte differentiation. Expression levels lower in smaller pig fetuses (PMID 21354690).	-
JAG1	rs6040076	20	10,658,882	*JAG1[N], MKKS[P]*	*JAG1:* Cerebellum and temporal cortex eQTL (proxy SNP)	*JAG1* is a ligand that interacts with receptors in the notch signalling pathway. Notch pathway plays an important role during placental development; notch pathway downregulation is associated with preeclampsia, and specifically JAG1 mRNA levels downregulated in preeclampsia placental samples vs controls (PMID 25962154).	-
C20orf203	rs28530618	20	31,275,581	*BAK1P1[E], FOXS1[P]*	*BAK1P1:* thyroid eQTL (for proxy SNP)		-

Locus	Lead SNP	Chr	Position (b37)	Candidate gene(s) in the locus[a]	Reports on eQTL[b]	Literature search for nearby genes (300kb)	Coding variants (EUR r^2 with the lead SNP)
MAFB	rs6016377	20	39,172,728	*MAFB[N], PLCG1[P]*	*MAFB:* Cerebellum and temporal cortex eQTL (for proxy SNP)	Lots of literature on importance of MAFB in transcriptional regulation in embryonic islets, e.g. analysis of Mafa(-/-) and pancreas-specific Mafa(Δpanc) deletion mutant mice demonstrated a primary role for MafA in adult β-cell activity, different from the embryonic importance of MafB (PMID 24520122).	-
NRIP1	rs2229742	21	16,339,172	*NRIP1[N,C], SAMSN1[P]*	*NRIP1:* Cerebellum and temporal cortex eQTL		rs2229742 (R448G, lead SNP, damaging)
KREMEN1	rs134594	22	29,468,456	*KREMEN1[N,E], YWHAH[P]*	*KREMEN1:* Monocyte, heart, whole blood, cerebellum and temporal cortex eQTL		-
SREBF2	rs62240962	22	42,259,524	*SREBF2[N,B], PDGFB[P]*			-
PLAC1	rs11096402	X	133,827,868	*PLAC1[N]*		*PLAC1* shows placenta-specific expression in human (PMID: 10995572). A mutant mouse model showed *PLAC1* as a paternally imprinted, X-linked gene essential for normal placental and embryonic development (PMID: 22729990).	-

[a]B = biological candidate, C = coding variant, E = eQTL (from GTEx), N=nearest, P = best ranked gene in PPI network, imp = imprinted gene.

[b]eQTL reported from GTEx v4, GEUVADIS, and 11 other studies for the lead variant. When there was no eQTL report for the lead variant, eQTL reports for the proxy SNPs (r^2>0.8 with the lead variant) are shown.

Supplementary Table 7. Summary of 99% credible sets at 62 distinct autosomal association signals.

Locus	Index variant	Chr	Position (b37, bp)	MANTRA $log_{10}BF$	99% credible set		
					Variants	Distance (bp)	Interval (bp)
WNT4-ZBTB40	rs2473248	1	22,536,643	7.68	7	17,534	22,536,643-22,554,176
ZBTB7B	rs3753639	1	154,986,091	12.19	6	22,088	154,984,363-155,006,450
	rs4330912	1	155,969,428	7.93	45	403,839	155,612,197-156,016,035
FCGR2B	rs72480273	1	161,644,871	7.48	37	173,221	161,500,712-161,673,932
DTL	rs61830764	1	212,289,976	6.02	56	702,234	211,830,044-212,532,277
ATAD2B	rs7575873	2	23,962,647	8.87	234	477,824	23,887,437-24,365,260
EPAS1	rs1374204	2	46,484,205	27.22	4	695	46,484,188-46,484,882
PTH1R	rs2242116	3	46,941,116	6.65	54	243,837	46,925,539-47,169,375
ADCY5	rs11719201	3	123,068,744	24.38	6	16,621	123,065,778-123,082,398
CPA3	rs10935733	3	148,622,968	7.91	80	33,654	148,591,725-148,625,378
CCNL1-LEKR1	rs13322435	3	156,795,468	40.24	11	3,265	156,795,468-156,798,732
LCORL	rs925098	4	17,919,811	13.56	15	123,806	17,901,679-18,025,484
HHIP	rs6537307	4	145,601,863	10.43	43	137,679	145,520,608-145,658,286
5q11.2	rs854037	5	57,091,783	5.77	63	276,269	56,906,160-57,182,428
EBF1	rs7729301	5	157,886,953	7.62	50	77380	157,884,706-157,962,085
CDKAL1	rs35261542	6	20,675,792	26.41	7	14,242	20,673,880-20,688,121
HIST1H2BE	rs9379832	6	26,186,200	6.64	5	26,542	26,180,634-26,207,175
HMGA1	rs9368777	6	33,788,637	6.20	91	570,460	33,292,543-33,863,002
	rs1187118	6	34,169,020	6.94	27	148,294	34,095,696-34,243,989
L3MBTL3	rs1415701	6	130,345,835	9.03	2	4,601	130,341,235-130,345,835
ESR1	rs1101081	6	152,032,917	17.69	14	20,968	152,029,556-152,050,523
GNA12	rs798489	7	2,801,803	7.01	114	160,777	2,752,152-2,912,928
IGF2BP3	rs11765649	7	23,479,013	7.58	23	111,149	23,474,687-23,585,835
TBX20	rs6959887	7	35,295,365	6.75	113	109,117	35,196,208-35,305,324
YKT6-GCK	rs138715366	7	44,246,271	24.10	1	1	44,246,271-44,246,271
MLXIPL	rs62466330	7	73,056,805	9.60	102	221,896	72,836,230-73,058,025
ANK1-NKX6-3	rs13266210	8	41,533,514	9.22	17	28,742	41,508,577-41,537,318
TRIB1	rs6989280	8	126,508,746	5.69	39	411,117	126,114,947-126,526,063
SLC45A4	rs12543725	8	142,247,979	7.18	10	13,200	142,239,381-142,252,580
PTCH1	rs12551019	9	96,949,079	6.96	40	652,934	96,900,505-97,553,438
	rs3780573	9	98,239,503	16.44	23	53,294	98,212,608-98,265,901

Locus	Index variant	Chr	Position	MANTRA	99% credible set		
			(b37, bp)	log_{10}BF	Variants	Distance (bp)	Interval (bp)
LPAR1	rs2150052	9	113,945,067	6.29	60	214,738	113,828,811-114,043,548
PHF19	rs7847628	9	123,631,225	6.95	5	90,924	123,631,225-123,722,148
STRBP	rs700059	9	125,824,055	10.35	135	432,744	125,605,840-126,038,583
HHEX-IDE	rs61862780	10	94,468,643	12.40	31	134,694	94,358,023-94,492,716
NT5C2	rs74233809	10	104,913,940	7.25	98	404,547	104,655,350-105,059,896
ADRB1	rs7076938	10	115,789,375	15.69	4	9,521	115,789,375-115,798,895
PLEKHA1	rs2421016	10	124,167,512	6.90	26	70,596	124,127,990-124,198,585
INS-IGF2	rs72851023	11	2,130,620	7.89	48	145,434	2,078,742-2,224,175
MTNR1B	rs10830963	11	92,708,710	5.78	52	499,464	92,225,858-92,725,321
APOLD1	rs11055034	12	12,890,626	6.33	13	42,180	12,849,241-12,891,420
ABCC9	rs139975827	12	22,068,161	5.64	72	133,773	22,027,182-22,160,954
ITPR2	rs12823128	12	26,872,730	6.12	114	291,548	26,759,026-27,050,573
HMGA2	rs1351394	12	66,351,826	30.74	7	32,282	66,343,810-66,376,091
IGF1	rs7964361	12	102,994,878	6.71	42	213,557	102,867,636-103,081,192
LINC00332	rs2324499	13	40,662,001	6.83	41	95,318	40,583,503-40,678,820
RB1	rs2854355	13	48,882,363	6.23	143	403,044	48,797,661-49,200,704
RNF219-AS1	rs1819436	13	78,580,283	7.44	105	220,228	78,443,297-78,663,524
FES	rs12906125	15	91,427,612	6.68	24	36,382	91,404,705-91,441,086
IGF1R	rs7402982	15	99,193,269	7.59	5	15,682	99,177,595-99,193,276
GPR139	rs1011939	16	19,992,996	7.20	55	53,120	19,992,996-20,461,115
CLDN7	rs113086489	17	7,171,356	13.41	29	84,570	7,101,292-7,185,861
SUZ12P1-CRLF3	rs144843919	17	29,037,339	7.60	21	520,396	28,780,178-29,300,573
SP6-SP2	rs12942207	17	45,968,294	7.04	21	90,685	45,940,310-46,030,994
ACTL9	rs61154119	19	8,787,750	6.24	21	4,455	8,785,744-8,790,198
PEPD	rs10402712	19	33,926,013	6.40	35	218,599	33,784,657-34,003,255
JAG1	rs6040076	20	10,658,882	6.72	43	164,577	10,539,775-10,704,351
C20orf203	rs28530618	20	31,275,581	8.69	63	114,192	31,214,234-31,328,425
MAFB	rs6016377	20	39,172,728	8.15	33	72,001	39,144,286-39,216,286
NRIP1	rs2229742	21	16,339,172	6.69	4	85,250	16,339,172-16,424,421
KREMEN1	rs134594	22	29,468,456	6.41	56	52,177	29,461,150-29,513,326
SREBF2	rs62240962	22	42,259,524	10.01	4	189,151	42,070,374-42,259,524

Chr, chromosome; bp, base pair; BF, Bayes factor.

Supplementary Table 8. BW credible set enrichment for DNaseI hypersensitive sites.

(a) 128 cell-type DHS annotation and 4 genic annotation tested for enrichment individually

Cell type	Lower 95%CI[a]	Effect[a]	Upper 95%CI[a]	Tissue	Category
iPS_6_9	-20.00	0.35	1.74	Stem cell	Stem cell
iPS_4_7	-20.00	0.82	2.04	Stem cell	Stem cell
iPS_19_7	-1.22	0.96	2.09	Stem cell	Stem cell
iPS_19_11	-1.40	0.80	1.93	Stem cell	Stem cell
hESCT0	-0.10	1.26	2.16	Stem cell	Stem cell
HESC	-20.00	0.21	1.79	Stem cell	Stem cell
NPC	0.94	2.14	2.99	Brain	Progenitor cell
HMVEC_dNeo	0.24	1.62	2.54	Neonatal blood vessel	Neonatal
HMVEC_dLyNeo	0.48	1.71	2.58	Neonatal blood vessel	Neonatal
HMVEC_dBlNeo	-0.82	1.00	2.01	Neonatal blood vessel	Neonatal
NHDF_Neo	1.22	2.29	3.12	Skin	Neonatal
fThymus	0.88	1.94	2.75	Foetal thymus	Foetal
fTestes	0.88	1.97	2.79	Foetal testes	Foetal
fStomach	0.40	1.63	2.50	Foetal stomach	Foetal
fSpleen	0.75	1.86	2.68	Foetal spleen	Foetal
fSpinal_cord	0.52	1.58	2.38	Foetal skin	Foetal
fSkin_fibro_upper_back	-0.86	1.43	2.44	Foetal skin	Foetal
fSkin_fibro_scalp	-4.83	1.03	2.17	Foetal skin	Foetal
fSkin_fibro_leg_R_quad	-20.00	0.84	2.11	Foetal skin	Foetal
fSkin_fibro_leg_L_quad	-0.89	1.23	2.25	Foetal skin	Foetal
fSkin_fibro_bicep_R	-20.00	0.73	2.05	Foetal skin	Foetal
fSkin_fibro_bicep_L	-20.00	1.09	2.24	Foetal skin	Foetal
fSkin_fibro_back	-20.00	0.04	1.75	Foetal skin	Foetal
fSkin_fibro_abdomen	-3.50	1.30	2.41	Foetal skin	Foetal
fSkin	-20.00	1.13	2.31	Foetal skin	Foetal
fPlacenta	0.80	1.72	2.49	Foetal placenta	Foetal
fMuscle_upper_trunk	0.70	1.74	2.55	Foetal muscle	Foetal
fMuscle_upper_limb_sk	-0.08	1.43	2.35	Foetal muscle	Foetal
fMuscle_upper_back	0.48	1.70	2.54	Foetal muscle	Foetal
fMuscle_trunk	0.63	1.72	2.54	Foetal muscle	Foetal
fMuscle_lower_limb	0.53	1.53	2.33	Foetal muscle	Foetal
fMuscle_leg	0.22	1.60	2.49	Foetal muscle	Foetal
fMuscle_back	0.34	1.37	2.17	Foetal muscle	Foetal
fMuscle_arm	0.46	1.73	2.60	Foetal muscle	Foetal
fLung_R	0.76	1.84	2.65	Foetal lung	Foetal
fLung_L	0.09	1.50	2.41	Foetal lung	Foetal
fLung	-1.03	1.34	2.42	Foetal lung	Foetal
fKidney_renal_pelvis_R	1.23	2.12	2.87	Foetal kidney	Foetal
fKidney_renal_pelvis_L	0.51	1.62	2.45	Foetal kidney	Foetal
fKidney_renal_pelvis	0.60	1.69	2.52	Foetal kidney	Foetal
fKidney_renal_cortex_R	0.03	1.44	2.35	Foetal kidney	Foetal
fKidney_renal_cortex_L	0.91	1.88	2.67	Foetal kidney	Foetal
fKidney_R	0.52	1.63	2.45	Foetal kidney	Foetal
fKidney_L	0.70	1.81	2.65	Foetal kidney	Foetal
fKidney	0.42	1.65	2.51	Foetal kidney	Foetal
fIntestine_Sm	-0.17	1.29	2.22	Foetal intestine	Foetal
fIntestine_Lg	0.25	1.63	2.55	Foetal intestine	Foetal
fHeart	0.21	1.56	2.45	Foetal heart	Foetal
fBrain	0.65	1.90	2.78	Foetal brain	Foetal

Cell type	Lower 95%_CI[a]	Effect[a]	Upper 95%_CI[a]	Tissue	Category
fAdrenal	0.54	1.69	2.52	Foetal adrenal	Foetal
WI_38_TAM	-3.99	0.83	1.95	Embryonic	Embryonic
WI_38	-20.00	0.43	1.87	Embryonic	Embryonic
Trophoblast	-20.00	1.21	2.36	Embryonic	Embryonic
Mesendoderm	-0.52	1.15	2.15	Embryonic	Embryonic
Skin_Melanocytes	-0.05	1.40	2.33	Skin	Adult
Skin_Keratinocytes	-20.00	0.84	2.00	Skin	Adult
Skin_Fibroblasts	0.81	1.81	2.64	Skin	Adult
NHEK	-20.00	0.57	1.98	Skin	Adult
NHDF_Ad	-0.75	1.09	2.09	Skin	Adult
BJ	-0.05	1.65	2.64	Skin	Adult
AG10803	-0.12	1.50	2.46	Skin	Adult
AG09309	-20.00	1.03	2.20	Skin	Adult
AG04449	-0.32	1.50	2.47	Skin	Adult
PrEC	-20.00	0.83	2.13	Prostate	Adult
LNCap	-20.00	1.28	2.42	Prostate	Adult
SkMC	-0.82	1.33	2.38	Muscle	Adult
HSMM_D	-20.00	0.66	1.83	Muscle	Adult
HSMM	-20.00	-1.29	1.31	Muscle	Adult
NHLF	-2.24	0.96	2.08	Lung	Adult
IMR90	-20.00	0.61	1.93	Lung	Adult
HPF	-1.69	1.00	2.10	Lung	Adult
AG04450	0.03	1.60	2.56	Lung	Adult
HRGEC	-0.64	1.57	2.60	Kidney	Adult
HCM	-20.00	0.79	1.99	Heart	Adult
HCFaa	-0.48	1.25	2.25	Heart	Adult
HCF	-2.09	1.13	2.20	Heart	Adult
HGF	0.49	1.88	2.79	Gingival	Adult
AG09319	-0.49	1.54	2.56	Gingival	Adult
HFF_MyC	-1.06	1.16	2.21	Foreskin	Adult
HFF	0.51	1.74	2.62	Foreskin	Adult
HConF	-20.00	0.94	2.12	Eye	Adult
SAEC	-20.00	0.92	2.11	Epithelium	Adult
RPTEC	-20.00	-0.11	1.55	Epithelium	Adult
HRPEpiC	-20.00	0.20	1.67	Epithelium	Adult
HRE	-1.34	1.17	2.20	Epithelium	Adult
HRCE	-20.00	0.82	2.02	Epithelium	Adult
HPdLF	-20.00	0.55	1.91	Epithelium	Adult
HNPCEpiC	-0.11	1.42	2.36	Epithelium	Adult
HIPEpiC	-0.16	1.38	2.32	Epithelium	Adult
HEEpiC	-0.05	1.51	2.45	Epithelium	Adult
HCPEpiC	0.06	1.53	2.45	Epithelium	Adult
HAEpiC	-0.87	1.21	2.23	Epithelium	Adult
HVMF	-0.07	1.53	2.49	Connective	Adult
vHMEC	-0.13	1.36	2.29	Breast	Adult
HMF	-0.37	1.35	2.31	Breast	Adult
HMEC	0.27	1.69	2.60	Breast	Adult
NHA	-1.48	1.16	2.22	Brain	Adult
HAsp	-20.00	0.63	1.91	Brain	Adult
HAh	-20.00	0.59	1.80	Brain	Adult
HAc	-20.00	0.63	1.97	Brain	Adult
HUVEC	-0.57	1.36	2.38	Blood vessel	Adult

Cell type	Lower 95%_CI[a]	Effect[a]	Upper 95%_CI[a]	Tissue	Category
HPAF	-20.00	0.95	2.08	Blood vessel	Adult
HPAEC	-1.23	1.34	2.44	Blood vessel	Adult
HMVEC_LLy	-0.39	1.32	2.34	Blood vessel	Adult
HMVEC_LBl	-4.39	0.70	1.90	Blood vessel	Adult
HMVEC_dLyAd	-20.00	1.02	2.24	Blood vessel	Adult
HMVEC_dBlAd	0.03	1.46	2.38	Blood vessel	Adult
HMVEC_dAd	-0.79	1.37	2.44	Blood vessel	Adult
HBMEC	-1.98	0.88	1.96	Blood vessel	Adult
AoAF	-20.00	0.73	1.92	Blood vessel	Adult
hTH2	0.28	1.54	2.43	Blood	Adult
hTH17	-20.00	1.00	2.39	Blood	Adult
hTH1	0.19	1.61	2.53	Blood	Adult
H9_P42	-0.80	1.24	2.27	Blood	Adult
H1_P18	-0.07	1.40	2.35	Blood	Adult
GM12878	-0.72	1.24	2.30	Blood	Adult
GM12865	-20.00	0.73	2.07	Blood	Adult
GM12864	-20.00	0.85	2.10	Blood	Adult
GM06990	-20.00	0.98	2.19	Blood	Adult
CD8	0.34	1.73	2.66	Blood	Adult
CD56	-1.01	1.06	2.13	Blood	Adult
CD4	-0.49	1.28	2.29	Blood	Adult
CD34	-0.15	1.50	2.49	Blood	Adult
CD3_CordBlood	-1.52	1.56	2.69	Blood	Adult
CD3	-2.48	1.09	2.30	Blood	Adult
CD20	-2.52	0.90	2.01	Blood	Adult
CD19	0.29	1.71	2.66	Blood	Adult
CD14	-0.70	1.07	2.10	Blood	Adult
TSS	-0.87	1.37	2.42	Genic	Genic
3UTR	-20.00	1.04	2.47	Genic	Genic
5UTR	-47.50	-2.00	2.14	Genic	Genic
CDS	-2.08	1.03	2.48	Genic	Genic

(b) Six categorical fields from ENCODE tested for enrichment in a joint model

Annotation	Lower 95% CI[a]	Effect[a]	Upper 95% CI[a]
Neonatal DHS	0.60	1.59	2.40
Foetal DHS	0.57	1.43	2.37
Genic	-0.85	0.63	1.61
Stem_cell DHS	-1.35	0.09	1.04
Adult DHS	-1.12	-0.26	0.62
Embryonic DHS	-3.95	-1.49	-0.39

[a]Estimated effects of enrichment and 95% CI are natural log transformed. We considered an annotation enriched if the 95% CI of the estimated effects of enrichment did not overlap zero.

Supplementary Table 9. Genetic variance explained.

Study	***N***	**By 62 known and novel SNPs**		**By 55 novel SNPs**	
		Variance explained	SE	Variance explained	SE
HAPO	1338	0.020	0.011	0.013	0.010
NFBC1966	5402	0.029	0.007	0.020	0.006
Generation R	2537	0.049	0.013	0.026	0.009

SE, standard error. HAPO study is independent of the birth weight meta-analysis whilst NFBC1966 and Generation R (European component) are part of the meta-analysis.

Supplementary Table 10. Look-up of maternal genotype effect on offspring BW (unadjusted for foetal genotype) in up to 68,254 mothers for the 60 BW loci detected in foetal birth weight GWAS.

Locus	Lead SNP	Allele		Foetal (European ancestry) GWAS		Maternal GWAS					Foetal Beta - Maternal Beta[a]
		Effect	Other	β	SE	EAF	β	SE	*P*-value	*N*	
WNT4-ZBTB40	rs2473248	C	T	0.033	0.006	0.88	0.013	0.010	0.20	48,632	0.020
ZBTB7B	rs3753639	C	T	0.031	0.004	0.25	0.017	0.008	0.03	48,632	0.014
FCGR2B	rs72480273	C	A	0.031	0.005	0.19	0.013	0.008	0.11	48,632	0.018
DTL	rs61830764	A	G	0.022	0.004	0.37	-0.002	0.007	0.76	48,632	0.020
ATAD2B	rs7575873	A	G	0.038	0.004	0.87	-0.011	0.010	0.27	48,632	0.028
EPAS1	rs1374204	T	C	0.047	0.004	0.69	0.024	0.006	$5.6x10^{-5}$	68,252	0.023
PTH1R	rs2242116	A	G	0.022	0.004	0.37	0.019	0.006	$9.3x10^{-4}$	67,542	0.004
ADCY5	rs11719201	T	C	0.046	0.004	0.25	-0.001	0.008	0.85	48,632	0.045
CPA3	rs10935733	T	C	0.022	0.004	0.40	0.015	0.007	0.02	48,632	0.007
CCNL1-LEKR1	rs13322435	A	G	0.053	0.004	0.59	0.026	0.006	$9.5x10^{-6}$	68,250	0.027
LCORL	rs925098	G	A	0.034	0.004	0.28	0.025	0.006	$2.9x10^{-5}$	68,254	0.009
HHIP	rs6537307	G	A	0.025	0.004	0.49	0.019	0.005	$4.4x10^{-4}$	68,247	0.006
5q11.2	rs854037	A	G	0.027	0.005	0.80	0.009	0.007	0.18	68,219	0.018
EBF1	rs7729301	A	G	0.024	0.004	0.74	0.039	0.007	$8.9x10^{-8}$	48,632	-0.015
CDKAL1	rs35261542	C	A	0.044	0.004	0.74	0.004	0.007	0.60	48,632	0.040
HIST1H2BE	rs9379832	A	G	0.023	0.004	0.73	0.008	0.007	0.30	48,632	0.015
HMGA1	rs7742369	G	A	0.028	0.005	0.19	0.017	0.007	0.01	68,253	0.011
L3MBTL3	rs1415701	G	A	0.025	0.004	0.73	0.037	0.006	$3.7x10^{-9}$	66,897	-0.012
ESR1	rs1101081	C	T	0.038	0.004	0.72	0.021	0.007	$3.8x10^{-3}$	48,632	0.017
GNA12	rs798489	C	T	0.023	0.004	0.72	0.023	0.006	$1.6x10^{-4}$	68,253	0.001
IGF2BP3	rs11765649	T	C	0.027	0.004	0.74	0.015	0.007	0.04	48,632	0.012
TBX20	rs6959887	A	G	0.023	0.004	0.61	0.009	0.006	0.10	68,232	0.014
YKT6-GCK	rs138715366	C	T	0.241	0.023	0.99	0.137	0.038	$2.8x10^{-4}$	48,632	0.104
MLXIPL	rs62466330	C	T	0.051	0.011	0.07	0.022	0.013	0.08	48,632	0.029
ANK1-NKX6-3	rs13266210	A	G	0.031	0.005	0.78	0.005	0.007	0.43	68,252	0.026
TRIB1	rs6989280	G	A	0.022	0.004	0.72	0.020	0.006	$1.3x10^{-3}$	67,520	0.003
SLC45A4	rs12543725	G	A	0.023	0.004	0.58	0.021	0.005	$1.4x10^{-4}$	68,222	0.002
PTCH1	rs28510415	G	A	0.056	0.007	0.09	0.034	0.011	$2.2x10^{-3}$	48,632	0.022
LPAR1	rs2150052	T	A	0.021	0.004	0.50	0.017	0.005	$1.4x10^{-3}$	68,245	0.004
PHF19	rs7847628	G	A	0.023	0.004	0.68	0.009	0.007	0.20	48,632	0.014
STRBP	rs700059	G	A	0.033	0.005	0.16	0.018	0.008	0.02	68,251	0.016

Locus	Lead SNP	Allele		Foetal (European ancestry) GWAS		Maternal GWAS					Foetal Beta - Maternal Beta[a]
		Effect	Other	β	SE	EAF	β	SE	*P*-value	*N*	
HHEX-IDE	rs61862780	T	C	0.028	0.004	0.49	-0.004	0.006	0.55	48,632	0.024
NT5C2	rs74233809	C	T	0.037	0.007	0.08	0.005	0.012	0.70	48,632	0.032
ADRB1	rs7076938	T	C	0.036	0.004	0.73	0.010	0.006	0.09	68,254	0.026
PLEKHA1	rs2421016	T	C	0.021	0.004	0.48	0.016	0.005	$3.3x10^{-3}$	68,253	0.005
INS-IGF2	rs72851023	T	C	0.048	0.008	0.08	0.015	0.012	0.24	48,632	0.033
MTNR1B	rs10830963	G	C	0.023	0.004	0.29	0.048	0.006	$5.1x10^{-15}$	67,603	-0.025
APOLD1	rs11055034	C	A	0.022	0.004	0.71	0.002	0.006	0.74	67,597	0.020
ABCC9	rs139975827	G	A	0.027	0.007	0.63	-0.010	0.007	0.13	48,632	0.017
ITPR2	rs12823128	T	C	0.021	0.004	0.53	0.009	0.005	0.08	68,187	0.012
HMGA2	rs1351394	T	C	0.044	0.004	0.49	0.034	0.005	$1.4x10^{-10}$	68,247	0.010
IGF1	rs7964361	A	G	0.039	0.007	0.10	0.018	0.010	0.06	68,251	0.021
LINC00332	rs2324499	G	C	0.022	0.004	0.68	0.012	0.006	0.05	68,213	0.011
RB1	rs2854355	G	A	0.023	0.004	0.26	0.017	0.007	0.03	48,632	0.007
RNF219-AS1	rs1819436	C	T	0.033	0.006	0.88	0.007	0.010	0.50	48,632	0.026
FES	rs12906125	G	A	0.023	0.004	0.68	0.029	0.007	$1.8x10^{-5}$	48,632	-0.006
IGF1R	rs7402982	A	G	0.023	0.004	0.41	0.021	0.007	$1.7x10^{-3}$	48,632	0.002
GPR139	rs1011939	G	A	0.022	0.004	0.28	0.007	0.007	0.34	48,632	0.015
CLDN7	rs113086489	T	C	0.031	0.004	0.54	0.022	0.007	$7.7x10^{-4}$	48,632	0.009
SUZ12P1-CRLF3	rs144843919	G	A	0.066	0.012	0.96	0.041	0.018	0.02	48,632	0.025
SP6-SP2	rs12942207	C	T	0.022	0.004	0.30	0.010	0.007	0.14	48,632	0.012
ACTL9	rs61154119	T	G	0.028	0.005	0.85	0.047	0.009	$1.5x10^{-7}$	48,632	-0.019
PEPD	rs10402712	A	G	0.022	0.004	0.26	-0.002	0.007	0.76	48,632	0.020
JAG1	rs6040076	C	G	0.023	0.004	0.51	0.015	0.007	0.02	48,632	0.008
C20orf203	rs28530618	A	G	0.026	0.004	0.47	0.003	0.006	0.62	48,632	0.023
MAFB	rs6016377	T	C	0.024	0.004	0.45	0.005	0.006	0.35	67,909	0.019
NRIP1	rs2229742	G	C	0.036	0.006	0.88	0.018	0.009	0.04	68,155	0.018
KREMEN1	rs134594	C	T	0.023	0.004	0.36	0.004	0.006	0.53	66,634	0.020
SREBF2	rs62240962	C	T	0.047	0.007	0.92	0.027	0.012	0.02	48,632	0.020
PLAC1	rs11096402	G	A	0.028	0.005	0.24	0.001	0.003	0.82	45,353	0.027

SE, standard error, EAF, effect allele frequency. The lead SNPs at *MTNR1B, HMGA2* and *L3MBTL3* attained genome-wide significance in the maternal, as well as the foetal GWAS. [a]Foetal GWAS effect size subtracted from maternal GWAS effect size: 55/60 beta values were more positive in the foetal GWAS (aligned to BW-raising allele) than in the maternal GWAS (2-tailed binomial sign test $P=1x10^{-11}$).

Supplementary Table 11. Maternal and foetal conditional analyses in 12,909 mother-child pairs.

Locus	Index variant	EA/ NEA	Maternal effect on offspring birth weight						Foetal effect on birth weight					
			Unadjusted			Adjusted for foetal genotype			Unadjusted			Adjusted for maternal genotype		
			β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value
WNT4-ZBTB40	rs2473248	C/T	0.004	0.018	0.82	-0.006	0.020	0.76	0.033	0.018	0.06	0.039	0.020	0.05
ZBTB7B	rs3753639	C/T	0.022	0.015	0.16	-0.005	0.017	0.79	0.060	0.016	$9.8x10^{-5}$	0.060	0.018	$5.7x10^{-4}$
FCGR2B	rs72480273	C/A	0.034	0.017	0.05	0.018	0.019	0.34	0.042	0.017	0.01	0.031	0.019	0.11
DTL	rs61830764	A/G	0.026	0.014	0.06	0.016	0.016	0.31	0.029	0.014	0.04	0.027	0.016	0.09
ATAD2B	rs7575873	A/G	0.018	0.019	0.35	0.007	0.022	0.74	0.042	0.019	0.03	0.047	0.022	0.03
EPAS1	rs1374204	T/C	0.032	0.013	0.02	0.008	0.015	0.60	0.056	0.013	$2.6x10^{-5}$	0.047	0.015	$1.9x10^{-3}$
PTH1R	rs2242116	A/G	0.025	0.013	0.05	0.031	0.015	0.03	0.002	0.013	0.86	-0.013	0.014	0.38
ADCY5	rs11719201	T/C	0.000	0.015	1.00	-0.025	0.017	0.15	0.057	0.015	$2.2x10^{-4}$	0.075	0.017	$1.5x10^{-5}$
CPA3	rs10935733	T/C	-0.004	0.013	0.73	-0.006	0.014	0.66	0.007	0.013	0.57	0.013	0.014	0.36
CCNL1-LEKR1	rs13322435	A/G	0.028	0.013	0.03	-0.015	0.014	0.31	0.091	0.013	$7.9x10^{-13}$	0.097	0.014	$9.7x10^{-12}$
LCORL	rs925098	G/A	0.012	0.014	0.39	-0.017	0.016	0.29	0.057	0.014	$3.1x10^{-5}$	0.060	0.015	$1.0x10^{-4}$
HHIP	rs6537307	G/A	0.028	0.013	0.03	0.003	0.014	0.85	0.057	0.013	$1.1x10^{-5}$	0.057	0.015	$7.8x10^{-5}$
5q11.2	rs854037	A/G	0.019	0.015	0.20	0.016	0.017	0.35	0.022	0.015	0.15	0.011	0.017	0.52
EBF1	rs7729301	A/G	0.036	0.014	$8.8x10^{-3}$	0.040	0.015	$9.6x10^{-3}$	0.024	0.014	0.08	0.010	0.016	0.52
CDKAL1	rs35261542	C/A	0.003	0.014	0.81	-0.028	0.016	0.07	0.057	0.014	$4.3x10^{-5}$	0.071	0.016	$6.1x10^{-6}$
HIST1H2BE	rs9379832	A/G	-0.005	0.014	0.74	-0.012	0.016	0.45	0.022	0.014	0.12	0.026	0.016	0.10
HMGA1	rs7742369	G/A	0.027	0.015	0.08	0.006	0.017	0.72	0.043	0.015	$4.9x10^{-3}$	0.035	0.017	0.04
L3MBTL3	rs1415701	G/A	0.035	0.014	0.01	0.019	0.016	0.22	0.052	0.014	$2.7x10^{-4}$	0.041	0.016	0.01
ESR1	rs1101081	C/T	0.009	0.014	0.51	-0.004	0.016	0.82	0.029	0.014	0.04	0.033	0.016	0.04
GNA12	rs798489	C/T	0.018	0.015	0.22	0.011	0.017	0.50	0.034	0.015	0.02	0.029	0.017	0.08
IGF2BP3	rs11765649	T/C	0.007	0.015	0.64	0.006	0.017	0.74	0.017	0.015	0.25	0.013	0.017	0.45
TBX20	rs6959887	A/G	0.018	0.013	0.15	-0.002	0.014	0.89	0.040	0.013	$1.7x10^{-3}$	0.036	0.014	0.01
YKT6-GCK	rs138715366	C/T	-0.030	0.087	0.73	-0.147	0.097	0.13	0.186	0.087	0.03	0.230	0.098	0.02
MLXIPL	rs62466330	C/T	0.019	0.028	0.50	-0.015	0.031	0.62	0.104	0.028	$2.2x10^{-4}$	0.129	0.031	$3.3x10^{-5}$
ANK1-NKX6-3	rs13266210	A/G	0.013	0.015	0.41	0.009	0.017	0.61	0.018	0.015	0.24	0.023	0.017	0.18
TRIB1	rs6989280	G/A	0.014	0.014	0.32	0.019	0.016	0.24	-0.003	0.014	0.84	-0.012	0.016	0.46
SLC45A4	rs12543725	G/A	0.012	0.013	0.36	0.004	0.015	0.79	0.013	0.013	0.31	0.014	0.015	0.34
PTCH1	rs28510415	G/A	0.037	0.023	0.11	-0.005	0.026	0.84	0.105	0.023	$8.0x10^{-6}$	0.105	0.027	$7.2x10^{-5}$
LPAR1	rs2150052	T/A	0.019	0.013	0.13	0.008	0.014	0.56	0.017	0.013	0.17	0.010	0.014	0.47
PHF19	rs7847628	G/A	0.020	0.013	0.13	0.018	0.015	0.24	0.022	0.013	0.11	0.017	0.015	0.25
STRBP	rs700059	G/A	0.017	0.016	0.27	-0.006	0.018	0.76	0.053	0.016	$8.0x10^{-4}$	0.062	0.018	$4.5x10^{-4}$
HHEX-IDE	rs61862780	T/C	0.012	0.013	0.36	-0.015	0.014	0.29	0.053	0.013	$3.0x10^{-5}$	0.059	0.014	$3.1x10^{-5}$

Locus	Index variant	EA/ NEA	Maternal effect on offspring birth weight						Foetal effect on birth weight					
			Unadjusted			Adjusted for foetal genotype			Unadjusted			Adjusted for maternal genotype		
			β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value
NT5C2	rs74233809	C/T	-0.002	0.021	0.94	-0.010	0.024	0.67	0.016	0.021	0.44	0.011	0.024	0.64
ADRB1	rs7076938	T/C	0.045	0.014	$8.8x10^{-4}$	0.032	0.015	0.03	0.050	0.014	$2.6x10^{-4}$	0.037	0.015	0.02
PLEKHA1	rs2421016	T/C	0.017	0.012	0.17	0.018	0.014	0.19	0.006	0.012	0.63	0.001	0.014	0.95
INS-IGF2	rs72851023	T/C	0.031	0.027	0.26	0.008	0.031	0.79	0.060	0.028	0.03	0.061	0.031	0.05
MTNR1B	rs10830963	G/C	0.047	0.015	$1.7x10^{-3}$	0.035	0.017	0.04	0.049	0.015	$9.8x10^{-4}$	0.032	0.017	0.06
APOLD1	rs11055034	C/A	-0.003	0.014	0.83	-0.013	0.016	0.42	0.005	0.014	0.72	0.011	0.016	0.51
ABCC9	rs139975827	G/A	0.005	0.014	0.72	-0.011	0.015	0.47	0.033	0.014	0.02	0.041	0.015	0.01
ITPR2	rs12823128	T/C	-0.003	0.013	0.83	-0.016	0.015	0.28	0.022	0.013	0.10	0.024	0.015	0.10
HMGA2	rs1351394	T/C	0.023	0.013	0.07	0.007	0.015	0.65	0.038	0.013	$3.0x10^{-3}$	0.038	0.014	0.01
IGF1	rs7964361	A/G	-0.005	0.023	0.85	-0.016	0.026	0.55	0.025	0.023	0.28	0.030	0.026	0.25
LINC00332	rs2324499	G/C	0.006	0.013	0.68	0.001	0.015	0.96	0.019	0.013	0.15	0.019	0.015	0.22
RB1	rs2854355	G/A	-0.013	0.015	0.37	-0.027	0.016	0.10	0.020	0.015	0.18	0.029	0.016	0.07
RNF219-AS1	rs1819436	C/T	0.040	0.018	0.03	0.013	0.020	0.52	0.057	0.018	$1.8x10^{-3}$	0.046	0.020	0.02
FES	rs12906125	G/A	0.006	0.014	0.66	-0.004	0.016	0.82	0.016	0.014	0.27	0.012	0.016	0.47
IGF1R	rs7402982	A/G	0.015	0.013	0.24	0.003	0.015	0.83	0.025	0.013	0.06	0.027	0.015	0.07
GPR139	rs1011939	G/A	0.015	0.014	0.27	0.013	0.015	0.39	0.008	0.014	0.57	0.000	0.015	1.00
CLDN7	rs113086489	T/C	0.018	0.013	0.16	0.002	0.014	0.89	0.043	0.013	$5.7x10^{-4}$	0.044	0.014	$1.9x10^{-3}$
SUZ12P1-CRLF3	rs144843919	G/A	0.003	0.037	0.93	-0.030	0.041	0.47	0.045	0.038	0.24	0.047	0.043	0.27
SP6-SP2	rs12942207	C/T	-0.001	0.014	0.92	-0.003	0.016	0.82	0.007	0.014	0.63	0.008	0.015	0.59
ACTL9	rs61154119	T/G	-0.005	0.016	0.75	-0.022	0.018	0.23	0.032	0.016	0.05	0.041	0.018	0.02
PEPD	rs10402712	A/G	-0.013	0.014	0.36	-0.028	0.016	0.07	0.016	0.014	0.26	0.025	0.016	0.11
JAG1	rs6040076	C/G	0.000	0.013	0.98	-0.007	0.015	0.64	0.010	0.013	0.43	0.017	0.015	0.24
C20orf203	rs28530618	A/G	0.015	0.013	0.23	0.013	0.014	0.34	0.006	0.013	0.63	0.003	0.014	0.85
MAFB	rs6016377	T/C	0.000	0.013	0.99	-0.021	0.015	0.16	0.042	0.013	$1.4x10^{-3}$	0.058	0.015	$9.9x10^{-5}$
NRIP1	rs2229742	G/C	0.026	0.023	0.26	0.018	0.026	0.49	0.031	0.023	0.17	0.018	0.026	0.49
KREMEN1	rs134594	C/T	0.016	0.013	0.22	0.007	0.015	0.64	0.017	0.013	0.20	0.015	0.015	0.30
SREBF2	rs62240962	C/T	0.019	0.026	0.47	0.005	0.029	0.87	0.049	0.026	0.06	0.049	0.029	0.09
PLAC1[a]	rs11096402	G/A	0.009	0.022	0.68	-0.004	0.024	0.88	0.013	0.024	0.60	0.014	0.027	0.61

[a]For analysis of the *PLAC1* locus on the X chromosome, we used female offsprings only: N = 4,940 mother-child pairs

EA: Effect Allele. NEA: Non Effect Allele. SE: standard error. Effects (beta values) are aligned to the BW-raising allele as reported in Extended Data Table 1a.

Supplementary Table 12. Summary results of LD Score regression analyses between birth weight and various diseases, metabolic and anthropometric traits.

(a) Birth weight and other traits

Phenotype1	Phenotype2	Genetic Correlation (r_g)	SE	z	*P*-value	Sample size of phenotype 2	Number of SNPs	Reference (PMID)
Birth weight	Infant head circumference	0.389	0.073	5.30	$1.2x10^{-7}$	10,770	1,019,674	22504419
Birth weight	Birth length	0.805	0.058	13.98	$2.0x10^{-44}$	28,460	983,823	25281659
Birth weight	Height (2014)	0.406	0.027	15.18	$4.8x10^{-52}$	253,300	1,049,262	25282103
Birth weight	Height (2010)	0.401	0.028	14.09	$4.6x10^{-45}$	133,900	1,026,905	20881960
Birth weight	Height (women)	0.400	0.032	12.59	$2.4x10^{-36}$	73,140	1,028,514	23754948
Birth weight	Height (men)	0.384	0.035	11.00	$3.7x10^{-28}$	60,590	1,024,139	23754948
Birth weight	Extreme height	0.399	0.043	9.20	$3.5x10^{-20}$	16,200	739,427	23563607
Birth weight	Body mass index (2015)	0.114	0.025	4.49	$7.3x10^{-6}$	322,200	1,050,986	25673413
Birth weight	Body mass index (2010)	0.120	0.033	3.66	$3.0x10^{-4}$	123,900	1,028,235	20935630
Birth weight	Extreme Body mass index	0.116	0.048	2.40	0.017	16,070	738,850	23563607
Birth weight	Body mass index (men)	0.148	0.040	3.67	$2.4x10^{-4}$	58,670	1,025,063	23754948
Birth weight	Body mass index (women)	0.096	0.035	2.76	0.006	67,960	1,029,327	23754948
Birth weight	Weight (men)	0.377	0.039	9.57	$1.1x10^{-21}$	58,350	1,025,155	23754948
Birth weight	Weight (women)	0.280	0.036	7.70	$1.4x10^{-14}$	67,590	1,029,320	23754948
Birth weight	Waist-hip ratio (2015)	-0.052	0.031	-1.66	0.097	212,200	1,048,211	25673412
Birth weight	Waist-hip ratio (adjusted for BMI - 2015)	-0.159	0.032	-4.93	$8.3x10^{-7}$	210,100	1,051,567	25673412
Birth weight	Waist-hip ratio (adjusted for BMI - 2010)	-0.189	0.041	-4.59	$4.4x10^{-6}$	77,220	1,027,370	20935629
Birth weight	Waist-hip ratio (men)	-0.080	0.053	-1.51	0.132	34,640	1,025,922	23754948
Birth weight	Waist-hip ratio (women)	-0.060	0.054	-1.11	0.268	42,730	1,029,620	23754948
Birth weight	Extreme waist-hip ratio	-0.254	0.071	-3.57	$3.6x10^{-4}$	10,260	674,047	23563607
Birth weight	Hip circumference	0.281	0.030	9.30	$1.4x10^{-20}$	213,000	1,048,111	25673412
Birth weight	Hip circumference (adjusted for BMI)	0.314	0.033	9.49	$2.3x10^{-21}$	211,100	1,049,874	25673412
Birth weight	Hip circumference (men)	0.339	0.063	5.34	$9.3x10^{-8}$	32,850	1,030,276	23754948
Birth weight	Hip circumference (women)	0.260	0.057	4.54	$5.6x10^{-6}$	40,360	1,031,503	23754948
Birth weight	Waist circumference	0.177	0.028	6.29	$3.9x10^{-10}$	232,100	1,048,634	25673412
Birth weight	Waist circumference (adjusted for BMI)	0.128	0.032	4.03	$5.7x10^{-5}$	231,400	1,049,871	25673412
Birth weight	Waist circumference (men)	0.218	0.053	4.11	$3.9x10^{-5}$	38,310	1,025,680	23754948
Birth weight	Waist circumference (women)	0.135	0.047	2.86	0.004	47,320	1,027,090	23754948
Birth weight	Obesity (class 1)	0.102	0.035	2.97	0.003	98,700	965,717	23563607
Birth weight	Obesity (class 2)	0.099	0.040	2.46	0.014	72,550	890,085	23563607

Phenotype1	Phenotype2	Genetic Correlation (r_g)	SE	z	*P*-value	Sample size of phenotype 2	Number of SNPs	Reference (PMID)
Birth weight	Obesity (class 3)	0.136	0.055	2.48	0.013	50,360	621,425	23563607
Birth weight	Childhood obesity	0.192	0.049	3.95	$7.8x10^{-5}$	13,850	1,057,303	22484627
Birth weight	Overweight	0.061	0.033	1.83	0.067	158,900	1,012,975	23563607
Birth weight	Anorexia nervosa	0.029	0.033	0.91	0.365	17,770	1,042,946	24514567
Birth weight	Crohn's disease	0.047	0.044	1.07	0.284	20,883	1,066,772	26192919
Birth weight	Irritable bowel syndrome	0.009	0.052	0.18	0.858	27,432	1,091,971	26192919
Birth weight	Rheumatoid arthritis	-0.004	0.046	-0.08	0.935	25,710	986,060	20453842
Birth weight	Lumbar spine bone mineral density	-0.027	0.043	-0.63	0.531	31,800	1,061,087	22504420
Birth weight	Lumbar spine bone mineral density (men)	-0.098	0.064	-1.53	0.127	9,980	1,060,919	22504420
Birth weight	Lumbar spine bone mineral density (women)	-0.003	0.044	-0.07	0.943	22,180	1,064,756	22504420
Birth weight	Femoral neck bone mineral density	0.013	0.039	0.34	0.736	32,960	1,065,335	22504420
Birth weight	Femoral neck bone mineral density (men)	-0.019	0.057	-0.33	0.745	9,971	1,056,535	22504420
Birth weight	Femoral neck bone mineral density (women)	0.020	0.050	0.40	0.686	22,990	1,069,031	22504420
Birth weight	Coronary artery disease	-0.295	0.051	-5.80	$6.5x10^{-9}$	84,270	932,642	21378990
Birth weight	Systolic blood pressure (adjusted for BMI)	-0.263	0.039	-6.72	$1.8x10^{-11}$	69,395	990,423	21909115
Birth weight	Systolic blood pressure (unadjusted for BMI)	-0.215	0.030	-7.21	$5.5x10^{-13}$	127,969	1,186,583	UK Biobank data
Birth weight	Diastolic blood pressure (adjusted for BMI)	-0.224	0.042	-5.35	$8.7x10^{-8}$	69,395	990,446	21909115
Birth weight	Triglycerides (2010)	-0.167	0.038	-4.41	$1.0x10^{-5}$	96,600	1,024,575	20686565
Birth weight	Triglycerides (2013)	-0.112	0.031	-3.61	$3.0x10^{-4}$	177,900	1,026,718	24097068
Birth weight	Total cholesterol (2010)	-0.127	0.040	-3.21	0.001	100,200	1,026,024	20686565
Birth weight	Total cholesterol (2013)	-0.105	0.033	-3.17	0.002	187,400	1,027,605	24097068
Birth weight	Low density lipoprotein (2010)	-0.136	0.047	-2.90	0.004	95,450	1,024,730	20686565
Birth weight	Low density lipoprotein (2013)	-0.102	0.036	-2.87	0.004	173,100	1,026,705	24097068
Birth weight	High density lipoprotein (2010)	0.087	0.039	2.23	0.026	99,900	1,026,029	20686565
Birth weight	High density lipoprotein (2013)	0.056	0.029	1.97	0.048	187,200	1,027,731	24097068
Birth weight	Type 2 diabetes	-0.271	0.056	-4.88	$1.1x10^{-6}$	69,030	976,437	22885922
Birth weight	Fasting insulin	-0.150	0.071	-2.10	0.036	46,190	1,054,692	20081858
Birth weight	Fasting insulin (adjusting for BMI)	-0.178	0.055	-3.26	0.001	51,750	1,121,151	22581228
Birth weight	HbA1c	-0.166	0.060	-2.75	0.006	46,368	1,109,233	20858683
Birth weight	2hr glucose	-0.245	0.094	-2.62	0.009	15,230	1,028,518	20081857
Birth weight	Fasting glucose	-0.073	0.054	-1.35	0.178	46,190	1,056,257	20081858
Birth weight	Fasting glucose (adjusting for BMI)	-0.126	0.048	-2.61	0.009	58,074	1,121,150	22581228
Birth weight	HOMA-IR	-0.133	0.072	-1.84	0.066	46,190	1,053,709	20081858
Birth weight	HOMA-B	-0.065	0.065	-1.00	0.317	46,190	1,053,581	20081858

Phenotype1	Phenotype2	Genetic Correlation (r_g)	SE	z	*P*-value	Sample size of phenotype 2	Number of SNPs	Reference (PMID)
Birth weight	Educational attainment (college)	0.111	0.042	2.63	0.009	126,600	1,017,448	25201988
Birth weight	Educational attainment (years)	0.105	0.043	2.43	0.015	126,600	1,014,207	25201988
Birth weight	Childhood intelligence	0.123	0.075	1.64	0.100	17,990	800,741	25201988
Birth weight	Autism	-0.089	0.053	-1.69	0.091	10,263	944,654	23453885
Birth weight	ADHD	-0.107	0.103	-1.04	0.300	3,351	1,065,753	20732625
Birth weight	Major depressive disorder	-0.076	0.074	-1.02	0.306	18,760	887,434	22472876
Birth weight	Bipolar disorder	0.026	0.047	0.56	0.578	16,730	800,584	21926972
Birth weight	Alzheimer's disease	-0.039	0.080	-0.49	0.622	74,050	1,142,332	24162737
Birth weight	Schizophrenia	-0.022	0.044	-0.49	0.624	21,860	846,564	21926974
Birth weight	Pubertal growth - height at age 10 in females and 12 in males - targets take-off phase of growth spurt	0.271	0.051	5.28	$1.3x10^{-7}$	13,960	1,009,067	23449627
Birth weight	Pubertal growth - height at age 12 in males	0.305	0.072	4.23	$2.3x10^{-5}$	6,986	1,017,307	23449627
Birth weight	Pubertal growth - height at age 10 in females	0.221	0.061	3.63	$3.0x10^{-4}$	6,974	1,036,441	23449627
Birth weight	Pubertal growth - total amount of growth across the pubertal growth period	0.162	0.062	2.61	0.009	10,800	1,037,500	23449627
Birth weight	Pubertal growth - total amount of growth across the pubertal growth period (males)	0.173	0.080	2.15	0.032	5,043	1,039,045	23449627
Birth weight	Pubertal growth - total amount of growth across the pubertal growth period (females)	0.142	0.083	1.70	0.089	5,756	1,038,734	23449627
Birth weight	Pubertal growth - total amount of growth in late adolescence, targeting the timing of peak height growth velocity	0.109	0.075	1.46	0.145	4,282	1,039,103	23449627
Birth weight	Pubertal growth - total amount of growth in late adolescence (males)	0.041	0.081	0.51	0.613	4,282	1,039,103	23449627
Birth weight	Pubertal growth - total amount of growth in late adolescence (females)	0.230	0.112	2.06	0.039	4,946	1,038,829	23449627
Birth weight	Age at menarche (2014)	0.029	0.031	0.93	0.354	133,000	1,057,631	25231870
Birth weight	Pubertal growth - Tanner scale	-0.137	0.125	-1.10	0.273	9,918	969,224	23449627
Birth weight	Pubertal growth - Tanner scale (males)	-0.453	0.650	-0.97	0.486	3,769	969,224	23449627
Birth weight	Pubertal growth - Tanner scale (females)	-0.037	0.138	-0.27	0.786	6,149	969,224	23449627
Birth weight	Asthma	0.050	0.069	0.72	0.471	10,770	1,019,674	20860503
Birth weight	Ever smoked	0.007	0.045	0.15	0.878	28,460	983,823	20418890
Birth weight	Former smoker	0.097	0.061	1.58	0.114	253,300	1,049,262	20418890
Birth weight	Cigarettes per day	-0.042	0.064	-0.67	0.505	133,900	1,026,905	20418890
Birth weight	Smoking start age	0.041	0.087	0.47	0.636	73,140	1,028,514	20418890

(b) Glucose-Related Phenotypes

Phenotype1	Phenotype2	Genetic Correlation (rg)	SE	z	*P*-value	Sample size of phenotype 2	Number of SNPs	Reference (PMID)
Type 2 diabetes	Fasting glucose	0.587	0.097	6.07	$1.3x10^{-9}$	46,190	1,056,257	20081858
Type 2 diabetes	2hr glucose	0.301	0.12	2.47	0.014	15,230	1,028,518	20081857
Type 2 diabetes	Fasting insulin	0.435	0.12	3.56	$4.0x10^{-4}$	46,190	1,054,692	20081858
Type 2 diabetes	HOMA-B	-0.002	0.11	-0.01	0.989	46,190	1,053,581	20081858

SE, standard error; BMI, body mass index; ADHD, attention deficit hyperactive disorder; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-B, homeostasis model assessment of beta cell function.

Supplementary Table 13. Estimating the proportion of the BW-adult phenotype covariance attributable to genotyped SNPs in UK Biobank and the Northern Finland Birth Cohort (NFBC) 1966 data.

Adult phenotype	*N*[a]	Phenotypic correlation with BW	Genetic correlation with BW (SE)	Residual correlation with BW (SE)	Genetic covariance with BW, gcov (SE)	Residual covariance with BW, rcov (SE)	Proportion of covariance explained by genetic variants directly genotyped: gcov/(gcov+rcov)[b] (95% CI)
UK Biobank							
Type 2 diabetes	56,654	-0.034	-0.124 (0.081)	-0.001 (0.010)	-0.012 (0.008)	-0.001 (0.008)	0.96 (0.36, 1.56)
Systolic blood pressure (unadjusted for BMI)	57,581	-0.072	-0.201 (0.037)	-0.011 (0.011)	-0.045 (0.008)	-0.008 (0.008)	0.85 (0.70, 0.99)
Systolic blood pressure (adjusted for BMI)	57,319	-0.084	-0.216 (0.030)	-0.042 (0.010)	-0.052 (0.007)	-0.031 (0.007)	0.62 (0.54, 0.71)
Diastolic blood pressure (adjusted for BMI)	57,230	-0.072	-0.156 (0.030)	-0.045 (0.010)	-0.038 (0.007)	-0.033 (0.007)	0.54 (0.44, 0.64)
Coronary artery disease	57,715	-0.002	-0.174 (0.182)	0.004 (0.009)	-0.008 (0.007)	0.003 (0.008)	N/A
Height	57,638	0.228	0.332 (0.026)	0.194 (0.015)	0.106 (0.008)	0.091 (0.007)	0.54 (0.50, 0.58)
Height (men)	23,385	0.202	0.343 (0.060)	0.214 (0.041)	0.108 (0.019)	0.090 (0.018)	0.55 (0.45, 0.64)
Height (women)	34,253	0.2	0.367 (0.037)	0.174 (0.029)	0.131 (0.013)	0.072 (0.012)	0.65 (0.58, 0.71)
Weight (men)	23,371	0.15	0.199 (0.074)	0.118 (0.027)	0.050 (0.018)	0.080 (0.018)	0.38 (0.24, 0.53)
Weight (women)	34,233	0.094	0.206 (0.049)	0.058 (0.019)	0.056 (0.013)	0.040 (0.013)	0.58 (0.45, 0.72)
Body mass index	57,402	0.043	0.063 (0.036)	0.031 (0.011)	0.014 (0.008)	0.023 (0.008)	0.39 (0.17, 0.61)
Body mass index (men)	34,077	0.045	0.049 (0.051)	0.019 (0.019)	0.013 (0.013)	0.013 (0.013)	0.49 (-0.01, 0.98)
Body mass index (women)	23,325	0.024	0.072 (0.087)	0.037 (0.025)	0.015 (0.018)	0.028 (0.018)	0.35 (-0.06, 0.77)
Obesity (class 1)	33,622	0.048	0.080 (0.051)	0.040 (0.020)	0.021 (0.013)	0.027 (0.013)	0.44 (0.17, 0.71)

Adult phenotype	*N*[a]	Phenotypic correlation with BW	Genetic correlation with BW (SE)	Residual correlation with BW (SE)	Genetic covariance with BW, gcov (SE)	Residual covariance with BW, rcov (SE)	Proportion of covariance explained by genetic variants directly genotyped: gcov/(gcov+rcov)[b] (95% CI)
Obesity (class 2)	23,846	0.028	0.016 (0.061)	0.050 (0.029)	0.005 (0.018)	0.032 (0.017)	0.13 (-0.37, 0.63)
Obesity (class 3)	20,966	0.01	-0.088 (0.105)	0.046 (0.026)	-0.017 (0.020)	0.036 (0.020)	N/A
Overweight	57,451	0.042	0.052 (0.045)	0.035 (0.010)	0.009 (0.008)	0.028 (0.008)	0.25 (0.04, 0.46)
Waist-hip ratio	57,590	0.077	-0.049 (0.041)	0.015 (0.010)	-0.010 (0.008)	0.012 (0.008)	N/A
Waist-hip ratio (adjusted for BMI)	57,388	0.065	-0.115 (0.042)	0.007 (0.010)	-0.022 (0.008)	0.005 (0.008)	N/A
Waist-hip ratio (men)	23,387	0.004	-0.081 (0.110)	0.026 (0.022)	-0.013 (0.018)	0.022 (0.018)	N/A
Waist-hip ratio (women)	34,203	-0.011	-0.023 (0.055)	-0.002 (0.018)	-0.006 (0.013)	-0.001 (0.013)	0.80 (-1.07, 2.68)
Waist circumference	57,641	0.103	0.084 (0.041)	0.091 (0.010)	0.017 (0.008)	0.072 (0.008)	0.19 (0.10, 0.28)
Waist circumference (adjusted for BMI)	57,435	0.129	0.147 (0.041)	0.008 (0.011)	0.029 (0.008)	0.006 (0.008)	0.83 (0.60, 1.05)
Waist circumference (men)	23,318	0.072	0.090 (0.089)	0.047 (0.025)	0.019 (0.018)	0.035 (0.018)	0.35 (0.01, 0.68)
Waist circumference (women)	34,252	0.014	0.083 (0.052)	0.017 (0.018)	0.021 (0.013)	0.012 (0.013)	0.63 (0.25, 1.01)
Hip circumference	57,559	0.066	0.173 (0.036)	0.033 (0.011)	0.039 (0.008)	0.025 (0.008)	0.61 (0.48, 0.73)
Hip circumference (adjusted for BMI)	57,359	0.070	0.292 (0.037)	0.015 (0.011)	0.065 (0.008)	0.011 (0.008)	0.85 (0.75, 0.96)
Hip circumference (men)	23,376	0.102	0.193 (0.082)	0.058 (0.026)	0.044 (0.018)	0.041 (0.018)	0.51 (0.30, 0.73)
Hip circumference (women)	34,183	0.046	0.146 (0.053)	0.026 (0.018)	0.037 (0.013)	0.019 (0.013)	0.66 (0.43, 0.89)
Age at menarche	33,518	0.022	0.021 (0.054)	0.008 (0.019)	0.005 (0.013)	0.006 (0.013)	0.49 (-0.72, 1.71)
Asthma	57,715	-0.019	-0.014 (0.054)	-0.007 (0.010)	-0.002 (0.008)	-0.006 (0.008)	0.25 (-0.67, 1.16)

Adult phenotype	*N*[a]	Phenotypic correlation with BW	Genetic correlation with BW (SE)	Residual correlation with BW (SE)	Genetic covariance with BW, gcov (SE)	Residual covariance with BW, rcov (SE)	Proportion of covariance explained by genetic variants directly genotyped: gcov/(gcov+rcov)[b] (95% CI)
Ever smoked	56,960	0.042	-0.011 (0.049)	0.043 (0.010)	-0.002 (0.008)	0.035 (0.008)	N/A
Former smoker	50,907	0.046	-0.038 (0.059)	0.048 (0.011)	-0.006 (0.009)	0.040 (0.009)	N/A
Cigarettes per day	50,641	0.044	-0.053 (0.052)	0.049 (0.011)	-0.009 (0.009)	0.040 (0.009)	N/A
Smoking start age	19,639	-0.024	0.465 (0.239)	-0.054 (0.024)	0.043 (0.020)	-0.048 (0.020)	N/A
NFBC1966							
Triglycerides	4,954	-0.065	-0.448 (0.224)	0.022 (0.049)	-0.083 (0.038)	0.018 (0.039)	N/A
Total cholesterol	4,970	-0.021	-0.271 (0.137)	0.080 (0.054)	-0.078 (0.039)	0.057 (0.038)	N/A
High density lipoprotein	4,972	0.020	0.101 (0.125)	-0.017 (0.055)	0.031 (0.039)	-0.011 (0.038)	N/A
Low density lipoprotein	4,970	-0.013	-0.223 (0.119)	0.093 (0.058)	-0.074 (0.039)	0.062 (0.038)	N/A
Fasting glucose	4,465	-0.042	-0.184 (0.173)	0.006 (0.058)	-0.045 (0.042)	0.005 (0.042)	N/A
Fasting insulin	4,441	-0.100	-0.180 (0.214)	-0.087 (0.056)	-0.036 (0.043)	-0.067 (0.043)	0.35 (-0.07, 1.28)

[a]The number of case/control was T2D: 1,488/55,166, CAD: 1,959/55,756, obesity1: 19,820/13,802, obesity2: 4,026/13,802, obesity3: 1,146/13,802, overweight: 37,631/19,820, asthma: 7,131/50,584, ever smoker: 24,774/32,186, and former smoker: 18,721/32,186 The covariance for these traits were on the observed scale.

[b]We have put N/A (not applicable) when the genetic and residual covariances are in the opposite direction and it is not relevant to calculate gcov/(gcov + rcov). Although genetic covariance is subject to high uncertainty, there is a general pattern across both UK Biobank and the NFBC1966 that the phenotypic covariation between low BW and future cardiometabolic risk is at least in part genetically mediated.

Supplementary Table 14. List of 77 reported imprinted regions used in the current analysis.

Gene	Type	Entrez ID	Chr	Gene Start site (bp, b37)	Gene End site (bp, b37)
CPA4	GTEX Primary	51200	7	129,932,973	129,964,020
CST1	GTEX Primary	1469	20	23,728,189	23,731,574
DIRAS3	GTEX Primary	9077	1	68,511,644	68,516,460
DLK1	GTEX Primary	8788	14	101,193,201	101,201,467
FAM50B	GTEX Primary	26240	6	3,849,631	3,851,551
GRB10	GTEX Primary	2887	7	50,657,759	50,861,159
H19	GTEX Primary	283120	11	2,016,405	2,019,065
IGF2	GTEX Primary	3481	11	2,150,346	2,170,833
IGF2AS	GTEX Primary	51214	11	2,161,757	2,169,896
INPP5F	GTEX Primary	22876	10	121,485,608	121,588,659
KCNQ1	GTEX Primary	3784	11	2,466,220	2,870,340
KIF25	GTEX Primary	3834	6	168,418,552	168,445,769
L3MBTL1	GTEX Primary	26013	20	42,136,319	42,170,534
LPAR6	GTEX Primary	10161	13	48,985,181	49,018,840
MAGEL2	GTEX Primary	54551	15	23,888,695	23,892,993
MAGI2	GTEX Primary	9863	7	77,646,373	79,082,890
MEG3	GTEX Primary	55384	14	101,292,444	101,327,360
MEG8	GTEX Primary	79104	14	101,361,106	101,373,305
MEST	GTEX Primary	4232	7	130,126,045	130,146,131
NAP1L5	GTEX Primary	266812	4	89,617,065	89,619,023
NDN	GTEX Primary	4692	15	23,930,553	23,932,450
NTM	GTEX Primary	50863	11	131,240,370	132,206,716
PEG10	GTEX Primary	23089	7	94,285,636	94,299,006
PEG3	GTEX Primary	5178	19	57,321,444	57,352,094
PLAGL1	GTEX Primary	5325	6	144,261,436	144,385,735
PPIEL	GTEX Primary	728448	1	39,987,951	40,025,370
PPP2R5D	GTEX Primary	5528	6	42,952,329	42,980,080
PWRN1	GTEX Primary	791114	15	24,803,303	24,832,926
SGK2	GTEX Primary	10110	20	42,187,634	42,214,273
SNRPN	GTEX Primary	6638	15	25,068,793	25,223,729
SNURF	GTEX Primary	8926	15	25,200,069	25,223,729
SYCE1	GTEX Primary	93426	10	135,367,403	135,382,876
UBE3A	GTEX Primary	7337	15	25,582,395	25,684,128
UGT2B4	GTEX Primary	7363	4	70,345,882	70,361,626
UTS2	GTEX Primary	10911	1	7,907,671	7,913,551
ZDBF2	GTEX Primary	57683	2	207,139,522	207,179,148
ZNF331	GTEX Primary	55422	19	54,024,176	54,083,523
ZNF597	GTEX Primary	146434	16	3,486,109	3,493,490
ABCA6	GTEX suggestive (S4 unique)	23460	17	67,074,846	67,138,015
BMP8A	GTEX suggestive (S4 unique)	353500	1	39,957,317	39,995,541
CHIT1	GTEX suggestive (S4 unique)	1118	1	203,185,206	203,198,860
DLGAP2	GTEX suggestive (S4 unique)	9228	8	1,449,568	1,656,642
DZIP1	GTEX suggestive (S4 unique)	22873	13	96,230,455	96,296,957
EMR1	GTEX suggestive (S4 unique)	2015	19	6,887,581	6,940,464
FKBP10	GTEX suggestive (S4 unique)	60681	17	39,968,961	39,979,469
GPR1	GTEX suggestive (S4 unique)	2825	2	207,040,041	207,082,771
GTSF1	GTEX suggestive (S4 unique)	121355	12	54,849,735	54,867,386
GUCY1B2	GTEX suggestive (S4 unique)	2974	13	51,568,646	51,640,293
KIR3DX1	GTEX suggestive (S4 unique)	90011	19	55,043,908	55,055,195
LRRTM1	GTEX suggestive (S4 unique)	347730	2	80,529,002	80,531,487

Gene	Type	Entrez ID	Chr	Gene Start site (bp, b37)	Gene End site (bp, b37)
MYOM2	GTEX suggestive (S4 unique)	9172	8	1,993,157	2,093,380
RTL1	GTEX suggestive (S4 unique)	388015	14	101,346,991	101,351,184
SERPINA6	GTEX suggestive (S4 unique)	866	14	94,770,584	94,789,688
SLC10A2	GTEX suggestive (S4 unique)	6555	13	103,696,347	103,719,196
THNSL2	GTEX suggestive (S4 unique)	55258	2	88,469,834	88,486,146
ANO1	GTEX consistent (S6)	55107	11	69,924,407	70,035,652
CALCR	GTEX consistent (S6)	799	7	93,053,798	93,204,042
CDKN1C	GTEX consistent (S6)	1028	11	2,904,447	2,906,995
COPG2	GTEX consistent (S6)	26958	7	130,146,079	130,353,598
DCN	GTEX consistent (S6)	1634	12	91,539,034	91,576,806
DIO3	GTEX consistent (S6)	1735	14	102,027,687	102,029,789
DLX5	GTEX consistent (S6)	1749	7	96,649,701	96,654,143
GABRA5	GTEX consistent (S6)	2558	15	27,111,865	27,194,357
GABRG3	GTEX consistent (S6)	2567	15	27,216,428	27,778,373
GLIS3	GTEX consistent (S6)	169792	9	3,824,127	4,300,035
GNAS-AS1	GTEX consistent (S6)	149775	20	57,393,972	57,425,958
KLF14	GTEX consistent (S6)	136259	7	130,417,395	130,418,888
MKRN3	GTEX consistent (S6)	7681	15	23,810,453	23,813,166
NNAT	GTEX consistent (S6)	4826	20	36,149,606	36,152,090
C15orf2	GTEX consistent (S6)	23742	15	24,920,540	24,928,593
PON3	GTEX consistent (S6)	5446	7	94,989,183	95,025,687
RB1	GTEX consistent (S6)	5925	13	48,877,882	49,056,026
RBP5	GTEX consistent (S6)	83758	12	7,276,279	7,281,466
SGCE	GTEX consistent (S6)	8910	7	94,214,535	94,285,521
TH	GTEX consistent (S6)	7054	11	2,185,158	2,193,035
TSPAN32	GTEX consistent (S6)	10077	11	2,323,242	2,339,430
TSSC4	GTEX consistent (S6)	10078	11	2,423,522	2,425,106

These 77 regions were highlighted in reference 10: Baran Y *et al*. *Genome Res* **25**, 927-936 (2015).

Supplementary Table 15. Comparison of variance in BW between individuals heterozygous and homozygous for each of the 59 autosomal BW index SNPs (plus *DLK1*) in 57,715 UK Biobank samples.

Locus	Index variant	Alleles	Variance			Effect		
		A/B	AA	AB	BB	β	SE	*P*-value
WNT4-ZBTB40	rs2473248	T/C	1.008	0.971	1.007	-0.015	0.006	0.99
ZBTB7B	rs3753639	T/C	0.994	1.004	1.026	0.002	0.005	0.34
FCGR2B	rs72480273	A/C	0.995	1.008	1.012	0.008	0.005	$6.4x10^{-2}$
DTL	rs61830764	G/A	0.997	0.993	1.031	-0.004	0.005	0.81
ATAD2B	rs7575873	A/G	1.007	0.978	0.964	-0.014	0.006	0.99
EPAS1	rs1374204	C/T	0.968	0.999	1.005	-0.002	0.005	0.68
PTH1R	rs2242116	A/G	1.003	0.987	1.013	-0.010	0.005	0.98
ADCY5	rs11719201	C/T	0.984	1.019	1.023	0.016	0.005	$1.1x10^{-3}$
CPA3	rs10935733	T/C	0.999	1.007	0.990	0.009	0.005	$3.7x10^{-2}$
CCNL1-LEKR1	rs13322435	A/G	1.016	0.993	0.981	-0.007	0.005	0.91
LCORL	rs925098	G/A	1.011	0.996	1.001	-0.002	0.005	0.64
HHIP	rs6537307	A/G	0.972	1.004	1.019	0.005	0.005	0.18
5q11.2	rs854037	A/G	1.004	0.990	1.008	-0.009	0.005	0.95
EBF1	rs7729301	G/A	1.028	0.990	1.003	-0.007	0.005	0.93
CDKAL1	rs35261542	C/A	1.004	0.998	0.969	$2x10^{-4}$	0.005	0.48
HIST1H2BE	rs9379832	A/G	1.004	0.995	0.995	-0.004	0.005	0.80
HMGA1	rs7742369	A/G	0.995	1.005	1.044	0.002	0.005	0.36
L3MBTL3	rs1415701	G/A	1.006	0.990	1.006	-0.009	0.005	0.96
ESR1	rs1101081	C/T	1.003	0.999	0.979	0.001	0.005	0.39
GNA12	rs798489	C/T	1.005	0.993	0.997	-0.005	0.005	0.81
IGF2BP3	rs11765649	T/C	1.004	0.991	1.007	-0.005	0.005	0.83
TBX20	rs6959887	A/G	0.998	1.001	0.999	0.004	0.005	0.21
YKT6-GCK	rs138715366	C/T	1.001	0.888	0.657	-0.070	0.019	1.00
MLXIPL	rs62466330	T/C	0.995	1.028	1.036	0.016	0.007	$1.3x10^{-2}$
ANK1-NKX6-3	rs13266210	A/G	1.007	0.984	1.009	-0.013	0.005	0.99
TRIB1	rs6989280	G/A	0.997	1.005	0.992	0.005	0.005	0.18
SLC45A4	rs12543725	G/A	1.009	0.994	0.999	-0.009	0.005	0.97
PTCH1	rs28510415	A/G	0.999	0.999	1.017	$1x10^{-4}$	0.007	0.49
LPAR1	rs2150052	A/T	0.980	1.002	1.015	0.002	0.005	0.37
PHF19	rs7847628	A/G	0.984	1.002	1.001	0.003	0.005	0.30
STRBP	rs700059	G/A	0.989	1.018	0.994	0.015	0.006	$4.4x10^{-3}$
HHEX-IDE	rs61862780	T/C	1.005	0.996	1.003	-0.005	0.005	0.82
NT5C2	rs74233809	T/C	0.999	0.998	1.136	$3x10^{-4}$	0.007	0.48
ADRB1	rs7076938	C/T	0.992	1.003	0.998	$6x10^{-4}$	0.005	0.45
PLEKHA1	rs2421016	C/T	0.988	1.007	0.998	0.008	0.005	$6.1x10^{-2}$
INS-IGF2	rs72851023	C/T	0.996	1.022	1.013	0.013	0.007	$3.4x10^{-2}$
MTNR1B	rs10830963	C/G	0.994	1.008	0.997	0.005	0.005	0.18
APOLD1	rs11055034	C/A	1.002	1.000	0.985	$2x10^{-4}$	0.005	0.49
ABCC9	rs139975827	G/A	1.006	1.000	0.982	$2x10^{-4}$	0.005	0.48
ITPR2	rs12823128	T/C	1.014	0.993	0.998	-0.006	0.005	0.87
HMGA2	rs1351394	T/C	1.003	1.001	0.993	$9x10^{-4}$	0.005	0.43
IGF1	rs7964361	G/A	0.999	1.006	0.991	0.003	0.007	0.35
LINC00332	rs2324499	G/C	1.000	0.998	1.004	-0.003	0.005	0.70
RB1	rs2854355	A/G	0.991	1.008	1.024	0.008	0.005	$5.4x10^{-2}$
RNF219-AS1	rs1819436	T/C	1.034	1.003	0.998	$5x10^{-4}$	0.006	0.47
DLK1	rs6575803	C/T	1.002	0.991	0.987	-0.007	0.006	0.87
FES	rs12906125	G/A	1.004	0.993	1.010	-0.005	0.005	0.86
IGF1R	rs7402982	A/G	0.994	0.998	1.006	-0.003	0.005	0.73

Locus	Index variant	Alleles A/B	Variance			Effect		
			AA	AB	BB	β	SE	*P*-value
GPR139	rs1011939	G/A	1.022	1.006	0.991	0.005	0.005	0.14
CLDN7	rs113086489	C/T	0.991	1.002	1.002	0.001	0.005	0.41
SUZ12P1-CRLF3	rs144843919	G/A	1.000	0.990	0.955	-0.006	0.010	0.72
SP6-SP2	rs12942207	C/T	1.018	1.005	0.992	0.006	0.005	0.12
ACTL9	rs61154119	T/G	0.998	1.007	0.974	0.003	0.006	0.30
PEPD	rs10402712	G/A	1.005	0.993	0.998	-0.004	0.005	0.78
JAG1	rs6040076	G/C	0.989	1.003	1.003	0.004	0.005	0.22
C20orf203	rs28530618	A/G	1.002	1.000	0.997	$4x10^{-4}$	0.005	0.47
MAFB	rs6016377	C/T	0.988	0.999	1.021	$2x10^{-4}$	0.005	0.48
NRIP1	rs2229742	G/C	1.002	0.991	0.939	-0.006	0.006	0.83
KREMEN1	rs134594	C/T	1.020	1.009	0.983	0.005	0.005	0.14
SREBF2	rs62240962	C/T	1.003	0.985	0.983	-0.008	0.007	0.89

The beta value is a parameter of the Brown-Forsythe test that measures how different the mean absolute deviations (MADs) are from the respective group medians in the heterozygous vs the homozygous group. SE, standard error.

Supplementary Table 16. Parent-of-origin specific analysis at 59 autosomal BW loci (plus *DLK1*) in 4,908 ALSPAC mother-child pairs.

Locus	SNP	EA/ NEA	Paternal transmission			Maternal transmission			*P*_het
			β	SE	*P*-value	β	SE	*P*-value	
WNT4-ZBTB40	rs2473248	C/T	0.019	0.042	0.65	0.189	0.076	$1.3x10^{-2}$	$6.1x10^{-2}$
ZBTB7B	rs3753639	C/T	0.012	0.034	0.72	0.078	0.045	$8.5x10^{-2}$	0.34
FCGR2B	rs72480273	C/A	0.097	0.037	$8.0x10^{-3}$	0.060	0.047	0.20	0.17
DTL	rs61830764	A/G	0.067	0.031	$2.8x10^{-2}$	0.096	0.030	$1.7x10^{-3}$	0.44
ATAD2B	rs7575873	A/G	0.080	0.041	$5.3x10^{-2}$	0.086	0.072	0.23	0.36
EPAS1	rs1374204	T/C	0.094	0.032	$3.7x10^{-3}$	0.121	0.037	$1.1x10^{-3}$	0.98
PTH1R	rs2242116	A/G	0.007	0.031	0.83	0.064	0.033	$5.2x10^{-2}$	$9.8x10^{-2}$
ADCY5	rs11719201	T/C	0.137	0.034	$4.5x10^{-3}$	0.062	0.035	$7.5x10^{-2}$	0.11
CPA3	rs10935733	T/C	0.052	0.029	$7.7x10^{-2}$	0.013	0.031	0.67	0.19
CCNL1-LEKR1	rs13322435	A/G	0.117	0.031	$1.4x10^{-4}$	0.088	0.032	$5.9x10^{-3}$	0.48
LCORL	rs925098	G/A	0.128	0.033	$1.1x10^{-4}$	0.063	0.042	0.13	0.18
HHIP	rs6537307	G/A	0.080	0.030	$8.1x10^{-3}$	0.071	0.030	$1.9x10^{-2}$	0.79
5q11.2	rs854037	A/G	0.078	0.037	$3.5x10^{-2}$	0.081	0.043	$5.8x10^{-2}$	0.90
EBF1	rs7729301	A/G	-0.006	0.034	0.86	-0.028	0.041	0.50	0.67
CDKAL1	rs35261542	C/A	0.101	0.033	$2.1x10^{-3}$	0.040	0.041	0.32	$8.3x10^{-2}$
HIST1H2BE	rs9379832	A/G	0.034	0.033	0.30	0.037	0.038	0.33	0.83
HMGA1	rs7742369	G/A	0.046	0.038	0.23	0.161	0.051	$1.6x10^{-3}$	0.10
L3MBTL3	rs1415701	G/A	0.029	0.033	0.38	0.092	0.042	$2.8x10^{-2}$	$9.2x10^{-2}$
ESR1	rs1101081	C/T	0.074	0.033	$2.5x10^{-2}$	0.025	0.039	0.53	0.16
GNA12	rs798489	C/T	0.011	0.033	0.74	0.043	0.040	0.29	0.35
IGF2BP3	rs11765649	T/C	-0.013	0.033	0.69	0.054	0.036	0.14	0.14
TBX20	rs6959887	A/G	0.035	0.032	0.27	0.035	0.033	0.29	0.94
YKT6-GCK	rs138715366	C/T	0.235	0.166	0.16	0.032	0.468	0.95	0.66
MLXIPL	rs62466330	C/T	0.107	0.053	$4.5x10^{-2}$	0.166	0.094	$7.8x10^{-2}$	0.87
ANK1-NKX6-3	rs13266210	A/G	0.039	0.036	0.28	-0.031	0.041	0.45	0.21
TRIB1	rs6989280	G/A	-0.012	0.034	0.73	0.018	0.040	0.66	0.60
SLC45A4	rs12543725	G/A	0.052	0.030	$8.6x10^{-2}$	0.047	0.030	0.12	0.90
PTCH1	rs28510415	G/A	0.091	0.047	$5.4x10^{-2}$	0.212	0.092	$2.1x10^{-2}$	0.39
LPAR1	rs2150052	T/A	-0.001	0.030	0.97	0.092	0.030	$2.0x10^{-3}$	$2.4x10^{-3}$
PHF19	rs7847628	G/A	0.038	0.032	0.23	0.004	0.037	0.92	0.28
STRBP	rs700059	G/A	0.043	0.041	0.29	-0.029	0.070	0.68	0.22
HHEX-IDE	rs61862780	T/C	0.085	0.030	$4.7x10^{-3}$	0.050	0.030	$9.6x10^{-2}$	0.32
NT5C2	rs74233809	C/T	-0.018	0.051	0.73	0.040	0.068	0.56	0.51
ADRB1	rs7076938	T/C	0.023	0.033	0.49	0.078	0.041	$5.5x10^{-2}$	0.27
PLEKHA1	rs2421016	T/C	0.024	0.031	0.43	0.036	0.031	0.24	0.77
INS-IGF2	rs72851023	T/C	0.116	0.051	$2.2x10^{-2}$	0.108	0.107	0.31	0.56
MTNR1B	rs10830963	G/C	0.024	0.033	0.46	0.058	0.040	0.15	0.53
APOLD1	rs11055034	C/A	0.122	0.032	$1.7x10^{-4}$	0.053	0.039	0.17	$3.2x10^{-2}$
ABCC9	rs139975827	G/A	0.045	0.031	0.15	0.017	0.032	0.59	0.46
ITPR2	rs12823128	T/C	0.064	0.030	$3.0x10^{-2}$	-0.003	0.029	0.91	$7.7x10^{-2}$
HMGA2	rs1351394	T/C	0.015	0.031	0.63	0.082	0.031	$8.3x10^{-3}$	$8.0x10^{-2}$
IGF1	rs7964361	A/G	-0.045	0.049	0.36	0.091	0.099	0.36	0.33
LINC00332	rs2324499	G/C	0.012	0.032	0.70	0.041	0.034	0.22	0.70
RB1	rs2854355	G/A	0.031	0.033	0.35	-0.012	0.042	0.77	0.25
RNF219-AS1	rs1819436	C/T	0.038	0.042	0.36	0.136	0.079	$8.4x10^{-2}$	0.39
DLK1	rs6575803	C/T	0.104	0.045	$2.2x10^{-2}$	0.205	0.091	$2.5x10^{-2}$	0.40
FES	rs12906125	G/A	0.019	0.032	0.55	0.095	0.035	$6.7x10^{-3}$	$9.3x10^{-2}$
IGF1R	rs7402982	A/G	0.047	0.031	0.13	0.036	0.032	0.25	0.78

Locus	SNP	EA/ NEA	Paternal transmission			Maternal transmission			*P*_het
			β	SE	*P*-value	β	SE	*P*-value	
GPR139	rs1011939	G/A	-0.028	0.032	0.38	0.021	0.038	0.59	0.29
CLDN7	rs113086489	T/C	0.061	0.031	$4.9x10^{-2}$	0.050	0.031	0.11	0.83
SUZ12P1-CRLF3	rs144843919	G/A	0.003	0.071	0.96	0.182	0.113	0.11	0.20
SP6-SP2	rs12942207	C/T	0.050	0.032	0.12	0.027	0.038	0.48	0.32
ACTL9	rs61154119	T/G	0.056	0.038	0.14	0.164	0.062	$8.7x10^{-3}$	$5.6x10^{-2}$
PEPD	rs10402712	A/G	0.077	0.033	$2.1x10^{-2}$	0.001	0.034	0.98	0.10
JAG1	rs6040076	C/G	0.028	0.031	0.36	0.001	0.031	0.97	0.53
C20orf203	rs28530618	A/G	0.053	0.031	$8.3x10^{-2}$	0.013	0.031	0.68	0.26
MAFB	rs6016377	T/C	0.054	0.031	$8.0x10^{-2}$	0.008	0.031	0.80	0.20
NRIP1	rs2229742	G/C	0.020	0.046	0.66	0.030	0.095	0.75	0.89
KREMEN1	rs134594	C/T	0.024	0.031	0.43	0.052	0.035	0.13	0.75
SREBF2	rs62240962	C/T	-0.004	0.052	0.94	0.088	0.065	0.18	0.40

EA, effect allele; NEA, non effect allele; SE, standard error; *P*_het, *P*-value for difference in BW between AB heterozygote offspring inheriting allele A from mother and B from father, and those inheriting A from father and B from mother.

Supplementary Table 17. Association of BW signals with various adult metabolic and anthropometric traits. (GWAS look-ups)

Provided in a separate Excel file.

Supplementary Table 18. Effect of transmitted and untransmitted maternal haplotype scores on BW in 5,201 ALSPAC mother-child pairs.

Haplotype score	Height			Systolic blood pressure			Type 2 diabetes		
	β	SE	*P*-value	β	SE	*P*-value	β	SE	*P*-value
M1 (C1)	0.128	0.013	$1.6x10^{-21}$	-6.82	3.36	0.04	-0.44	1.73	0.80
M2	0.010	0.012	0.39	-6.40	2.63	0.02	1.66	1.42	0.24
C2	0.066	0.012	$1.2x10^{-7}$	0.14	2.62	0.96	-2.94	1.47	0.045

Beta values are in grams per weighted trait-raising allele. SE, standard error.
M1(C1), maternal transmitted haplotype score; M2, Maternal untransmitted haplotype score; C2, paternal transmitted haplotype score.

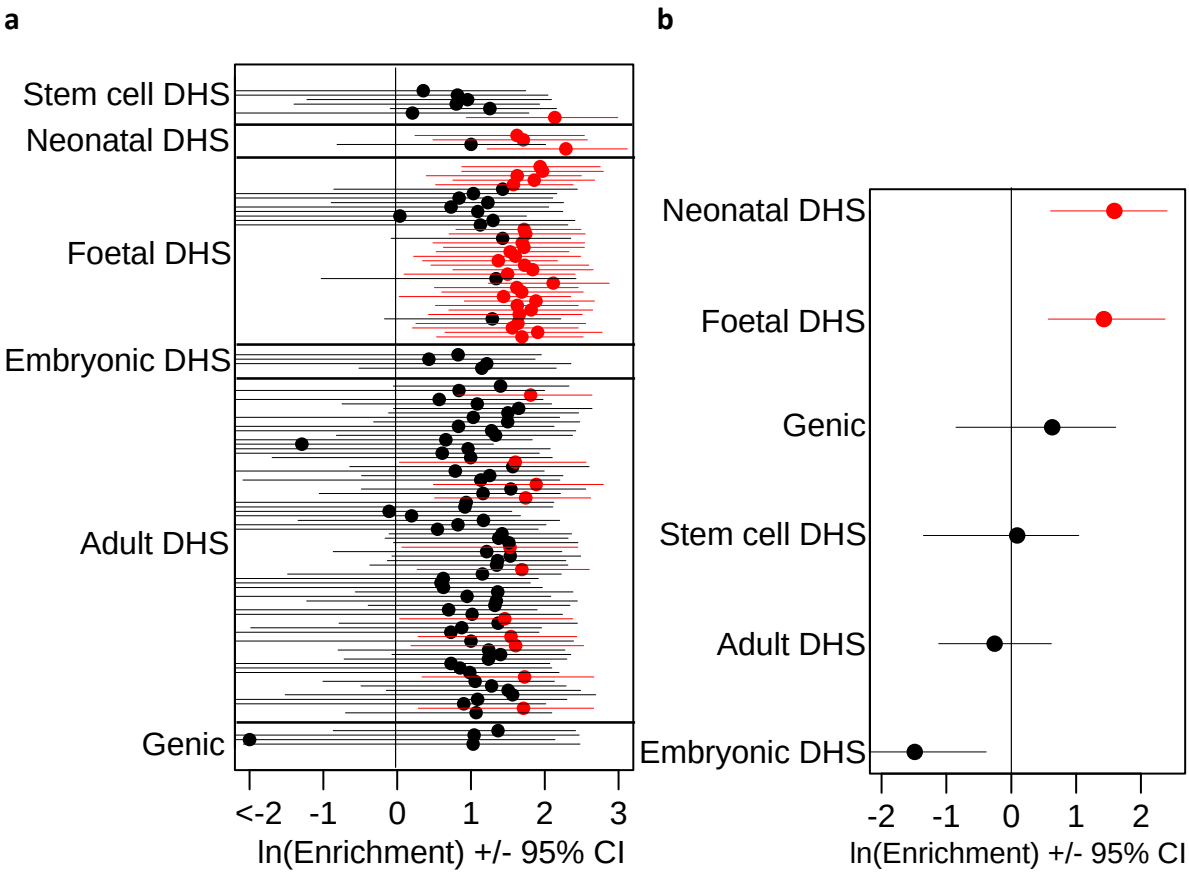
Supplementary Table 19. Reciprocal approximate conditional analyses at *YKT6-GCK* variants associated with birth weight (BW) or fasting glucose (FG), in European ancestry meta-analysis of up to 143,677 individuals.

Variant (chr:position)	Type	EA/ NEA	EAF (Eur)	BW SNP conditioned on FG SNP				FG SNP conditioned on BW SNP			
				Unconditioned *P*	Conditioned on	Variant type	Conditioned *P*	Variant	Conditioned on	Unconditioned *P*	Conditioned *P*
rs138715366 (7:44246271)	BW lead SNP (at *YKT6* intron 1)	T/C	0.0089	$7.2x10^{-26}$	unconditioned	-	-	-	-	-	-
					rs878521	*GCK* FG primary (ENGAGE[1])	$1.3x10^{-25}$	rs878521	rs138715366	0.12	0.28
					rs10259649	*GCK* FG secondary (ENGAGE[1])	$7.7x10^{-26}$	rs10259649	rs138715366	0.52	0.63
					rs4607517	*GCK* FG (MAGIC[2])	$2.6x10^{-25}$	rs4607517	rs138715366	$3.2x10^{-4}$	$1.2x10^{-3}$
					rs10278336	*GCK* T2D (DIAGRAM[3])	$1.8x10^{-25}$	rs10278336	rs138715366	0.057	0.19
rs78412508 (7:44223858)	BW second strongest SNP (at *GCK* intron 3)	A/G	0.0095	$8.9x10^{-24}$	unconditioned	-	-	-	-	-	-
					rs878521	*GCK* FG primary (ENGAGE[1])	$1.6x10^{-23}$	rs878521	rs78412508	0.12	0.27
					rs10259649	*GCK* FG secondary (ENGAGE[1])	$9.7x10^{-24}$	rs10259649	rs78412508	0.52	0.66
					rs4607517	*GCK* FG (MAGIC[2])	$3.1x10^{-23}$	rs4607517	rs78412508	$3.2x10^{-4}$	$1.2x10^{-3}$
					rs10278336	*GCK* T2D (DIAGRAM[3])	$2.2x10^{-23}$	rs10278336	rs78412508	0.057	0.18

EA, effect allele; NEA, non effect allele, EAF, effect allele frequency; Eur, European; BW, birth weight; FG, fasting glucose; T2D, type 2 diabetes.

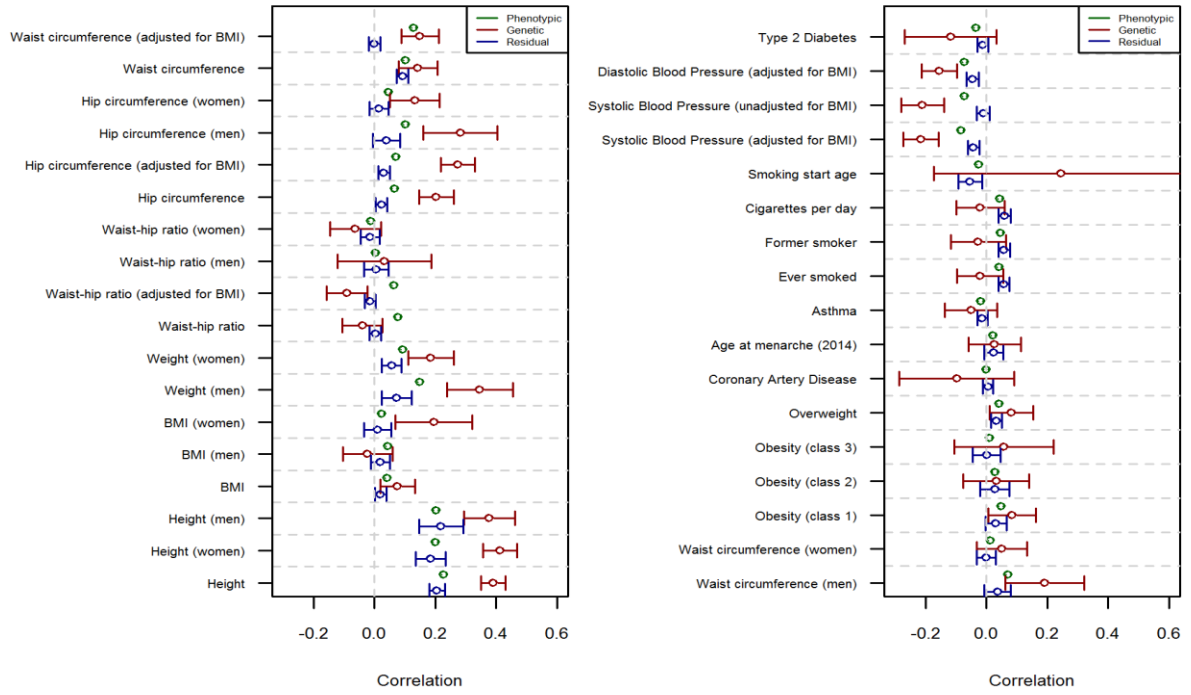
1. Horikoshi M *et al*. PLoS Genet 11, e1005230 (2015).
2. Dupuis J *et al*. Nat Genet 42, 105-116 (2010).
3. Morris AP *et al*. Nat Genet 44, 981-990 (2012).

Supplementary Figure 1. BW association enrichment for DNaseI hypersensitive (DHS) sites in 128 cell types and four genic annotations. a, Each cell type DHS annotation and four gene-based annotations were individually tested for enrichment using the Bayes Factors for all variants in the 62 credible sets. The effect estimate (filled circle) and 95% CI (horizontal line) are plotted on the *x* axis. The 128 cell types (listed on the *y* axis; see Supplementary Table 8 for details) are categorised according to the description fields from ENCODE (stem cell, neonatal, foetal, embryonic and adult groups). We considered an annotation enriched if the 95% CI did not overlap zero (highlighted in red). **b,** Estimated effect of enrichment (filled circle) and 95% CI (horizontal line) for each categorical field, tested in a joint model, are plotted (see Methods).

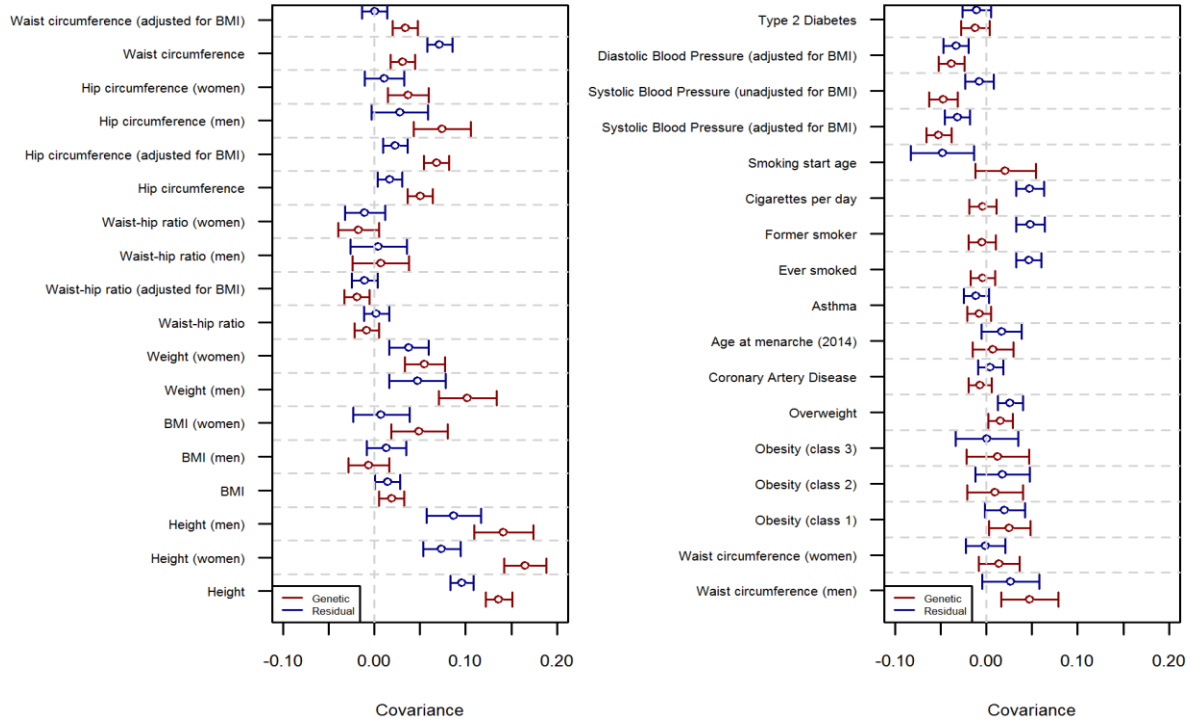


Supplementary Figure 2. Estimates of phenotypic, genetic and residual correlations (a) and estimates of genetic and residual covariance (b) between birth weight and adult metabolic or anthropometric traits in UK Biobank 'white British' samples (up to N=57,715). See details in Supplementary Table 13.

a



b



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Regional association plots for birth weight

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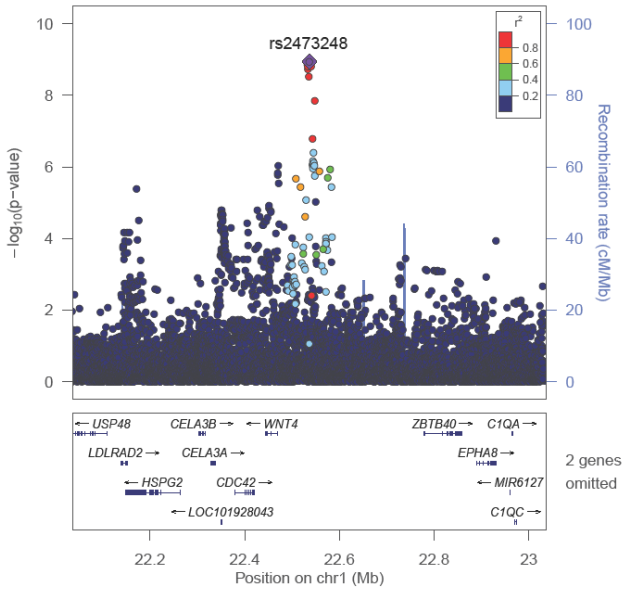

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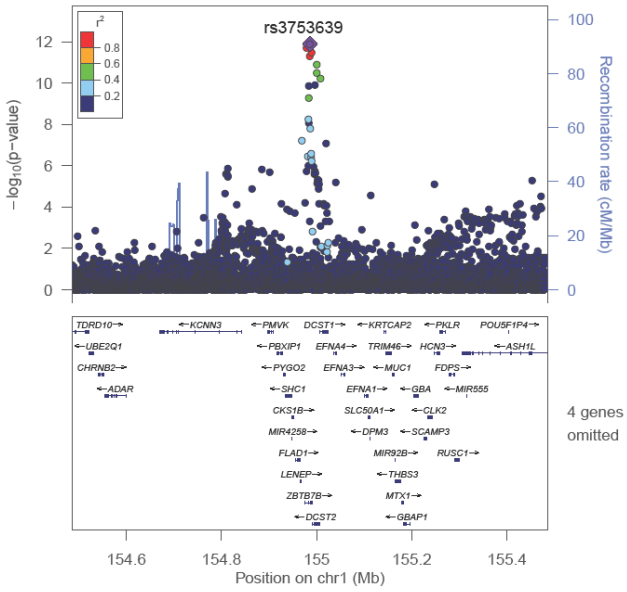

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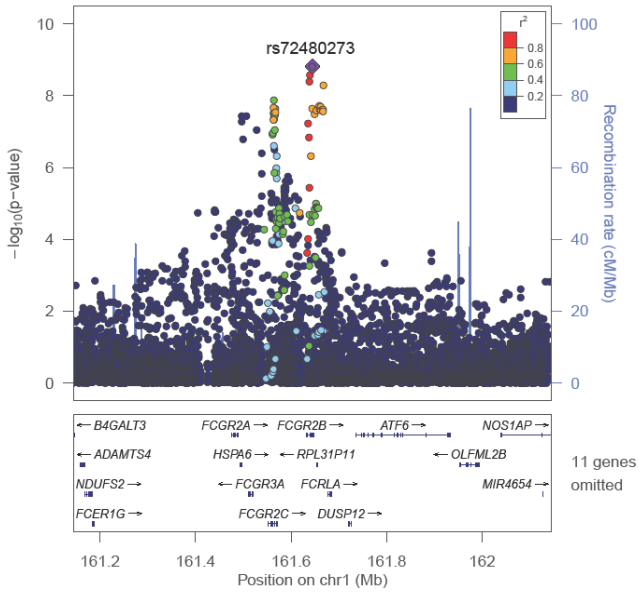

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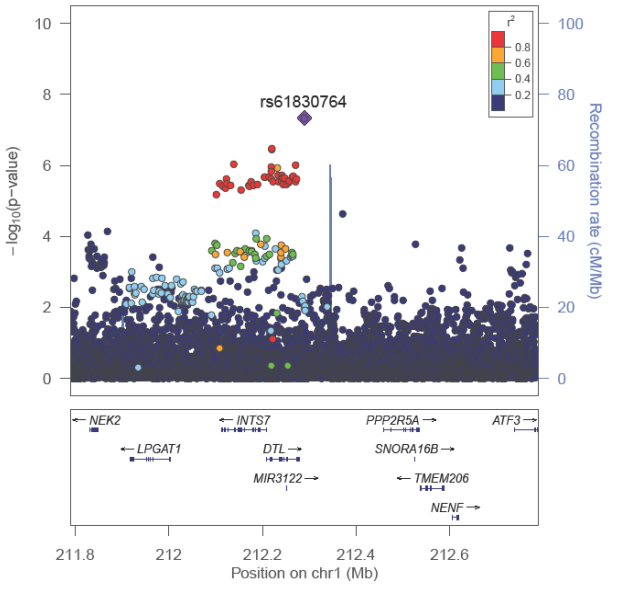

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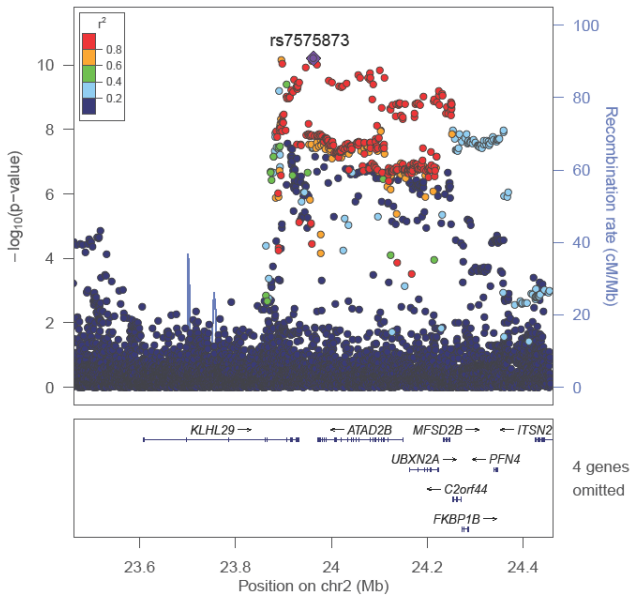

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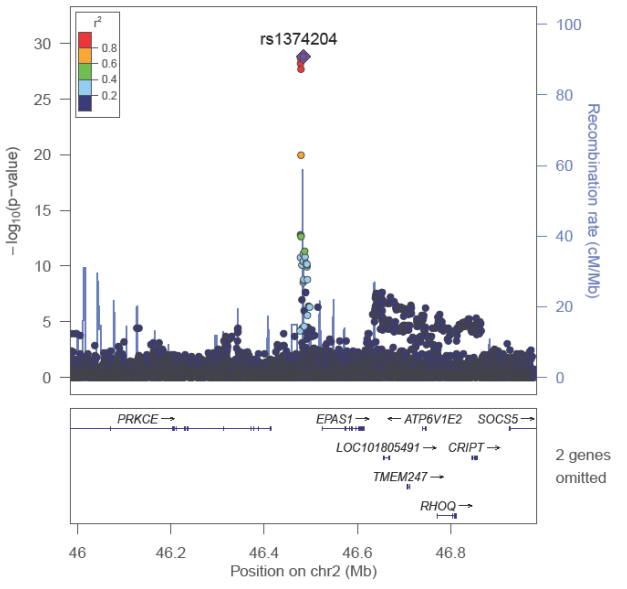

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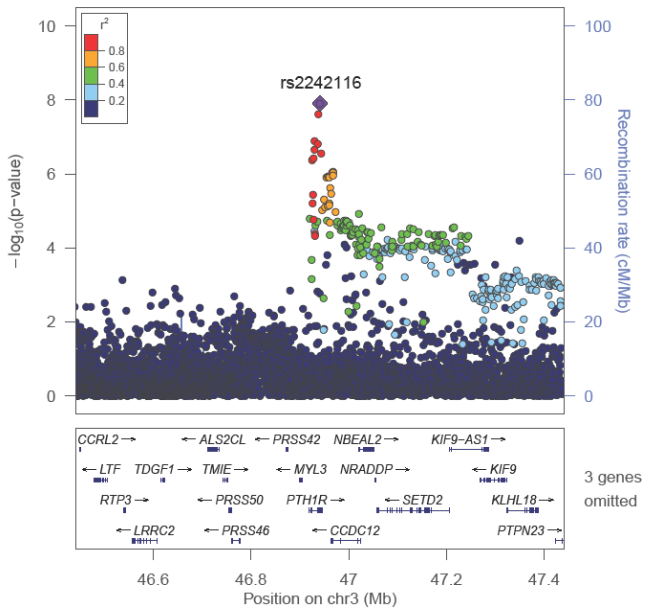

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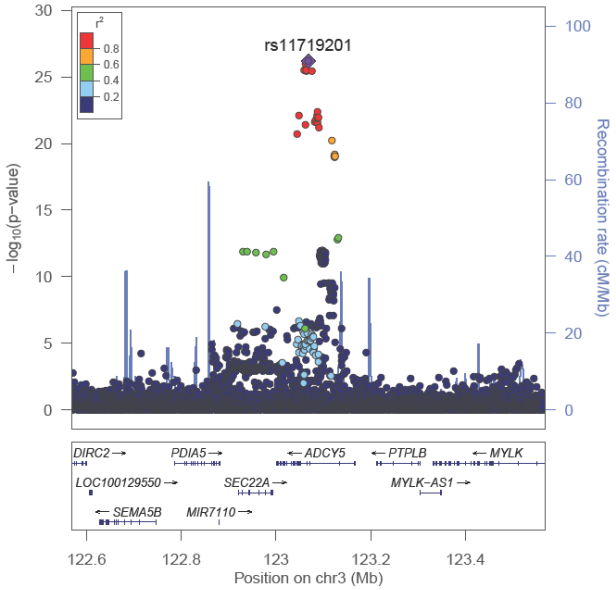

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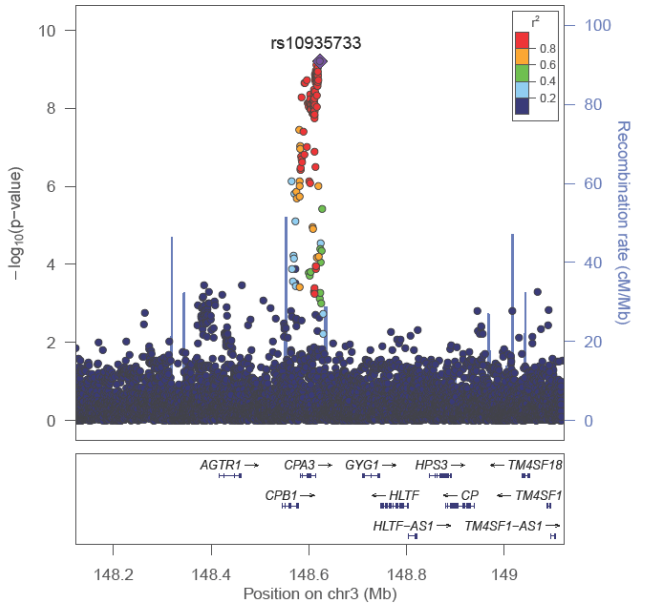

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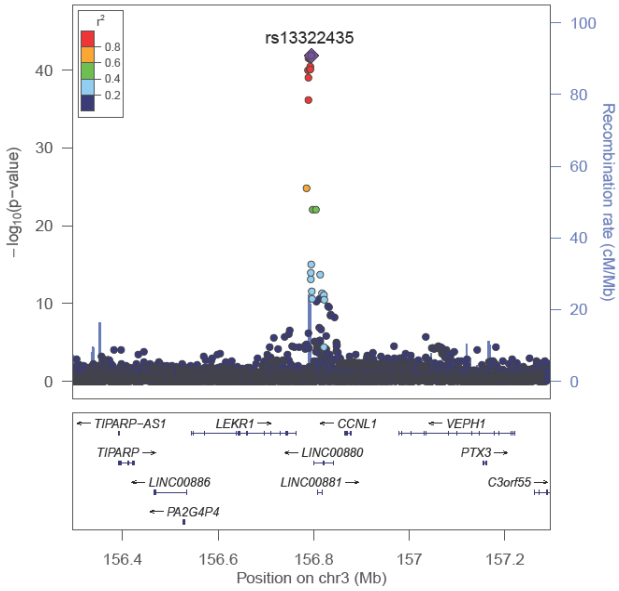

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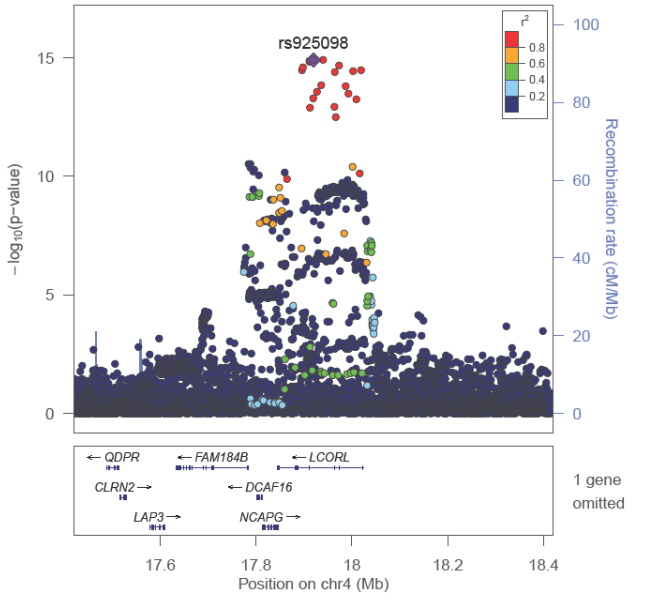

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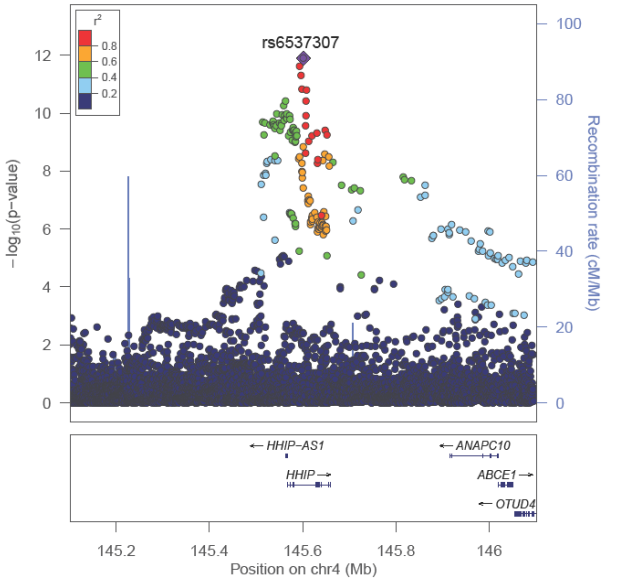

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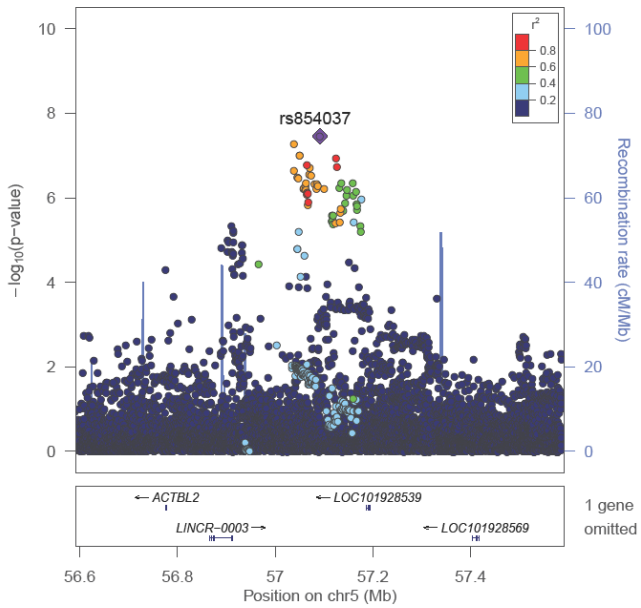

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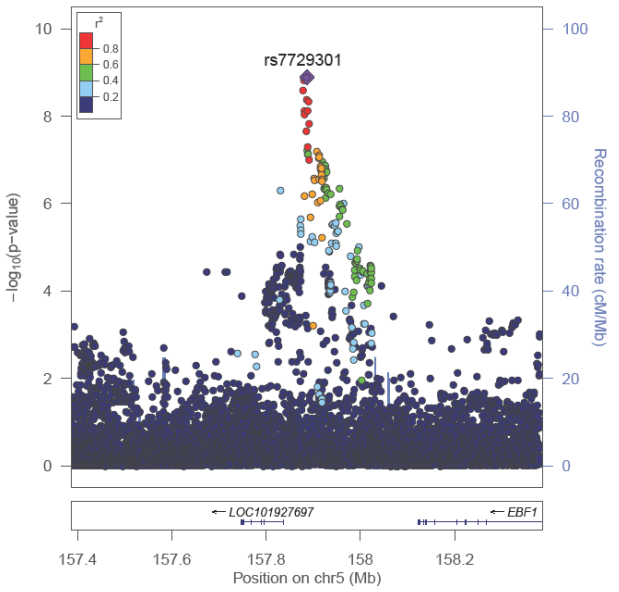

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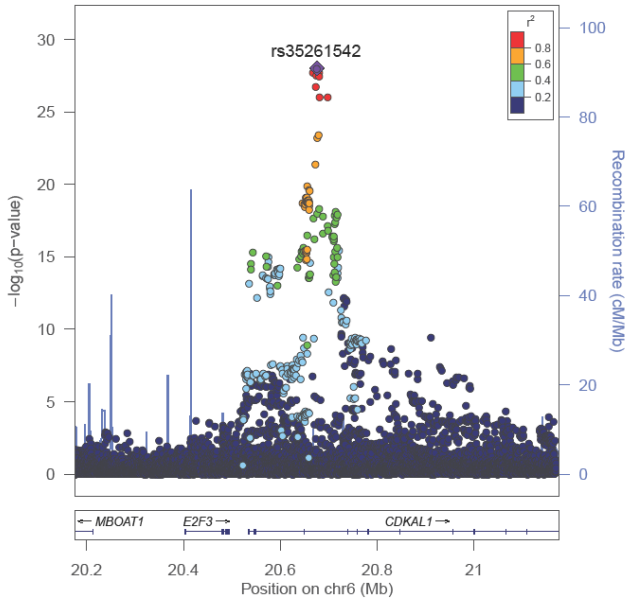

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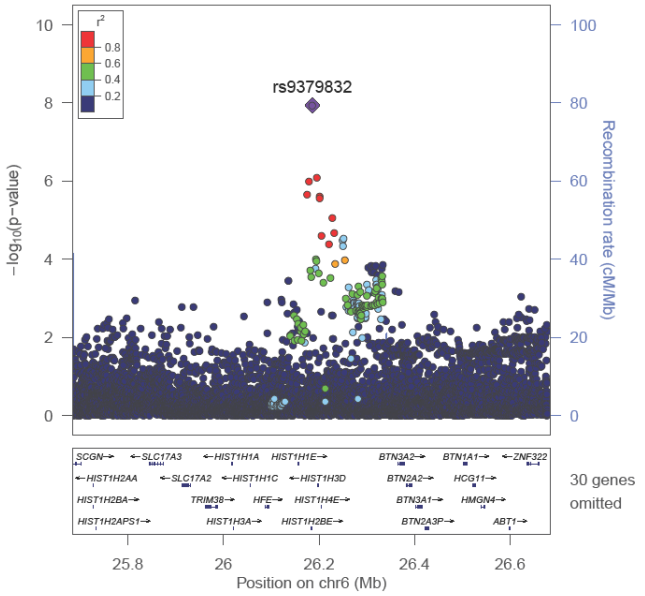

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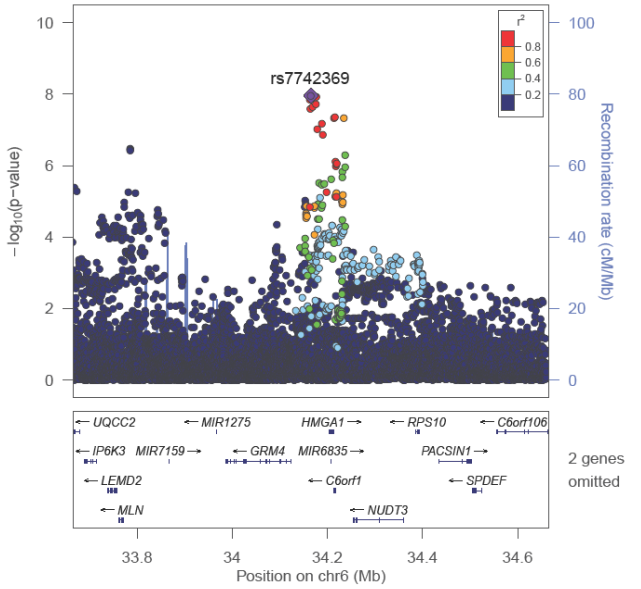

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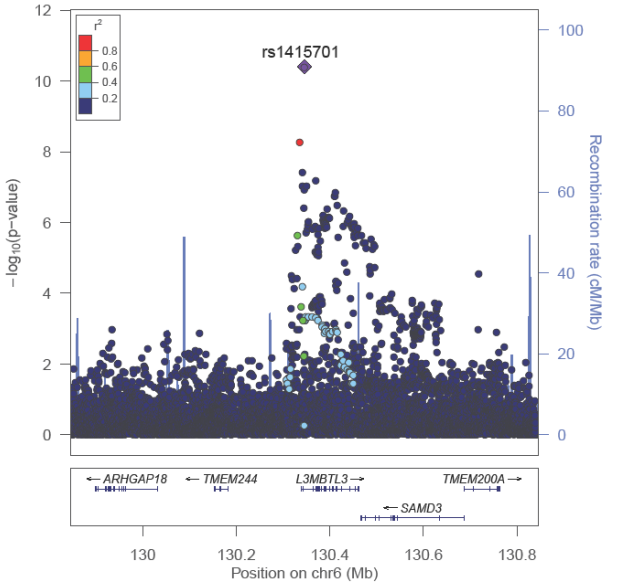

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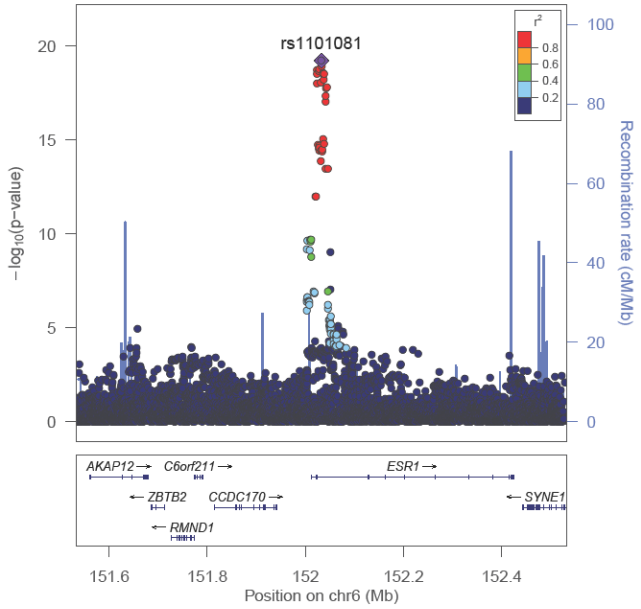

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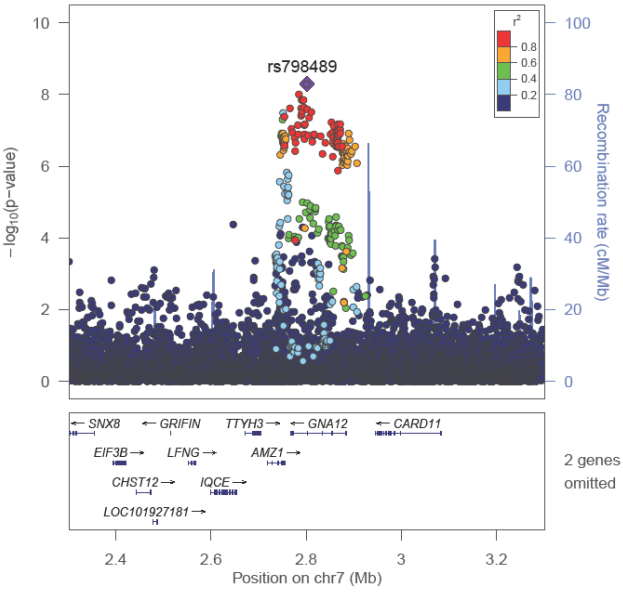

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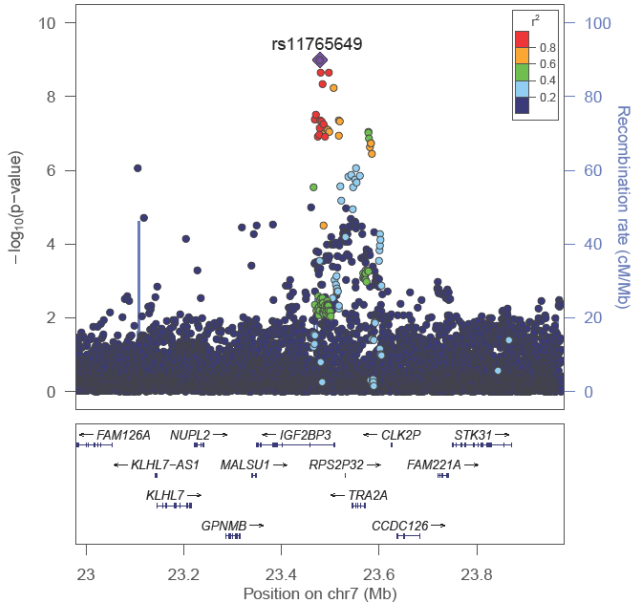

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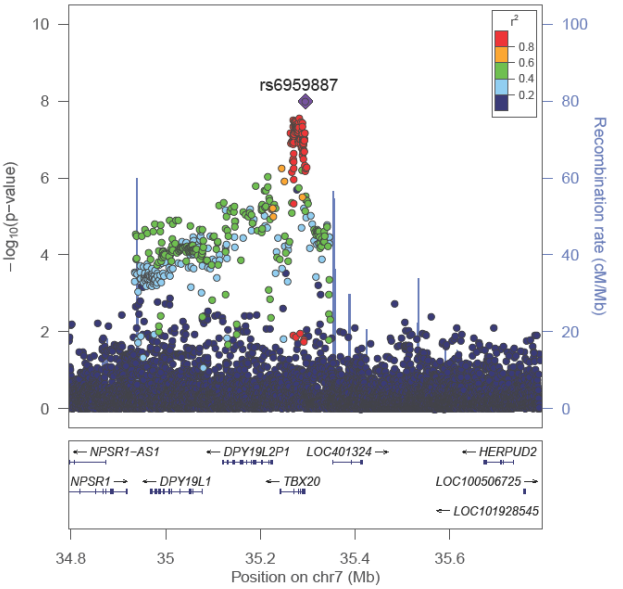

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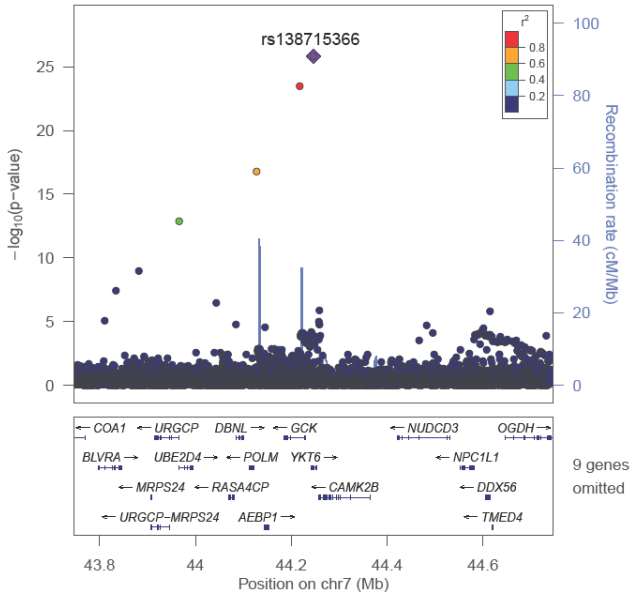

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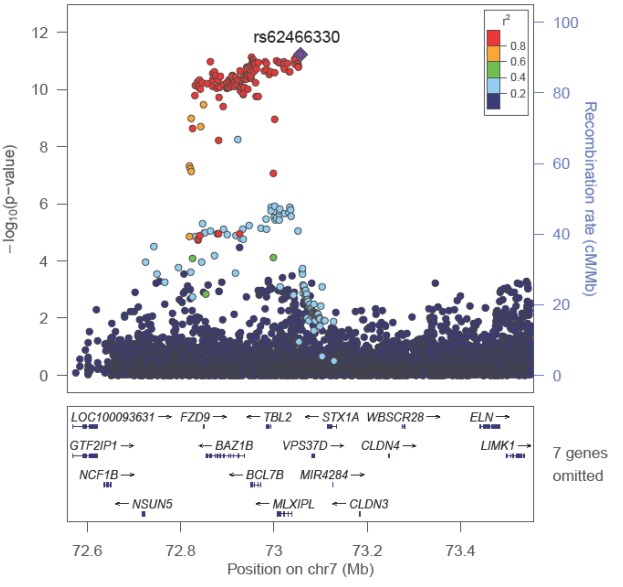

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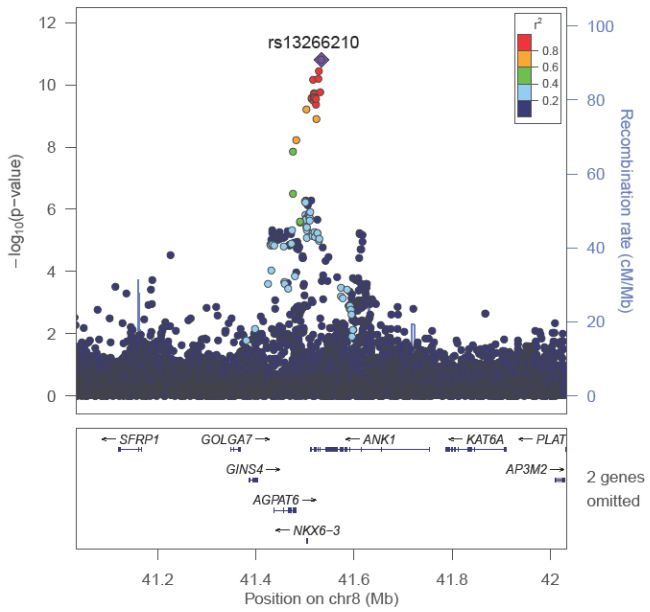

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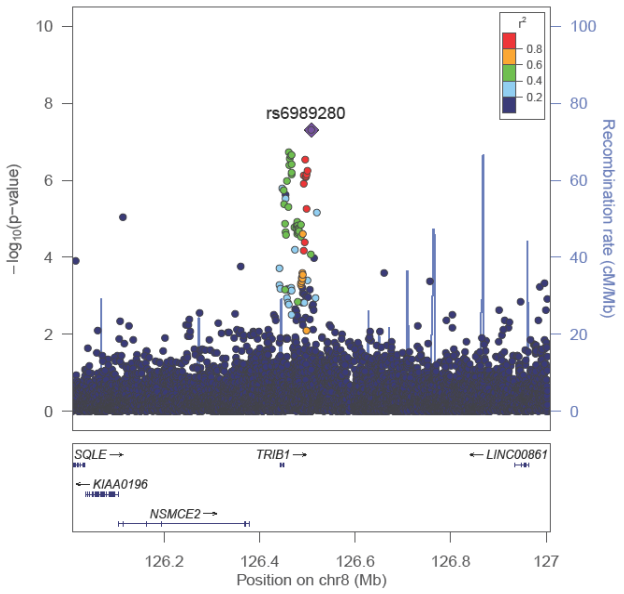

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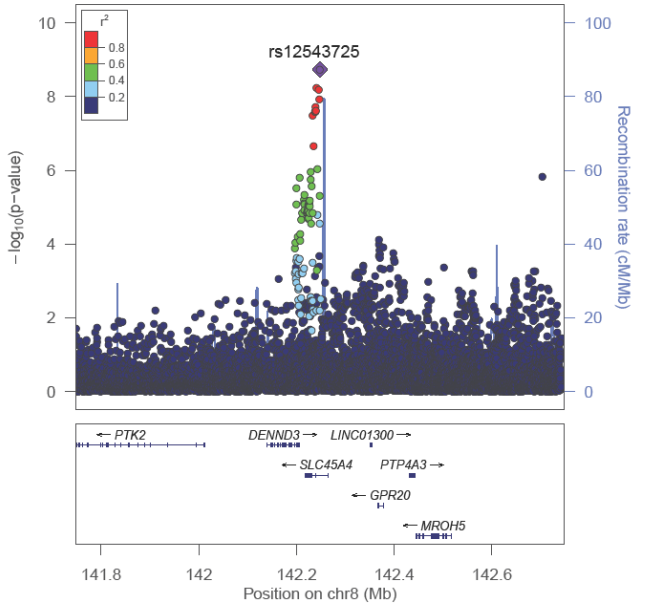

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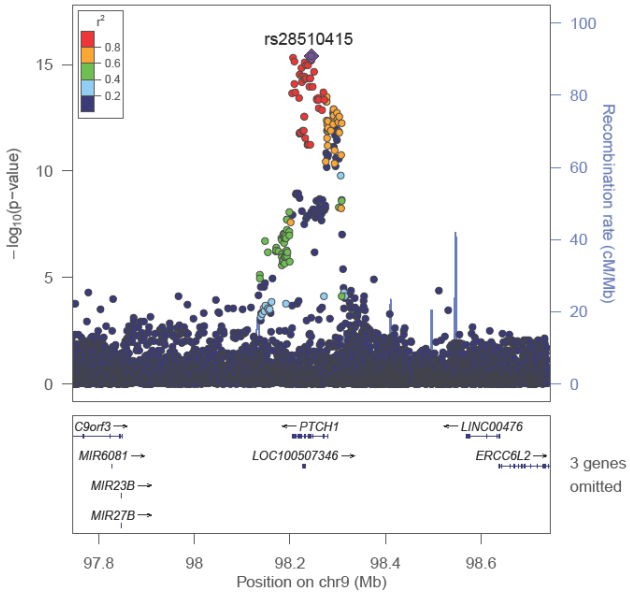

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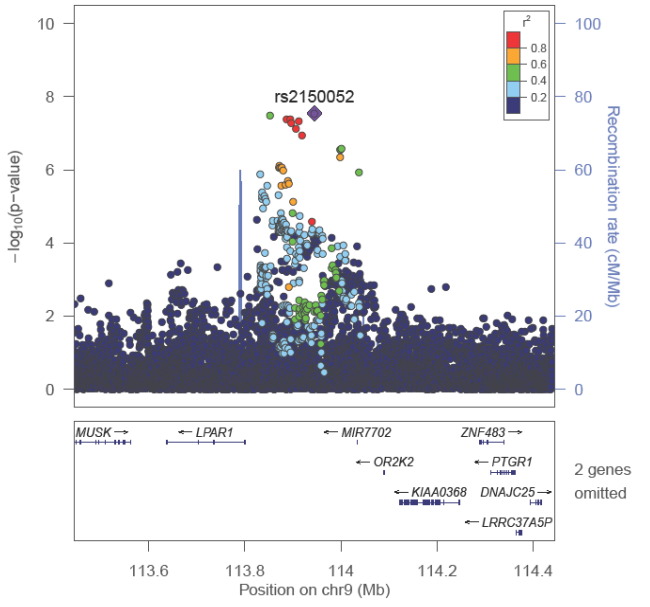

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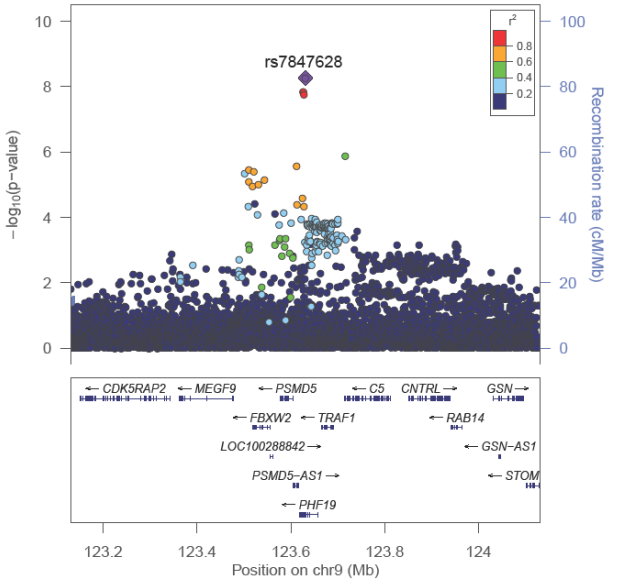

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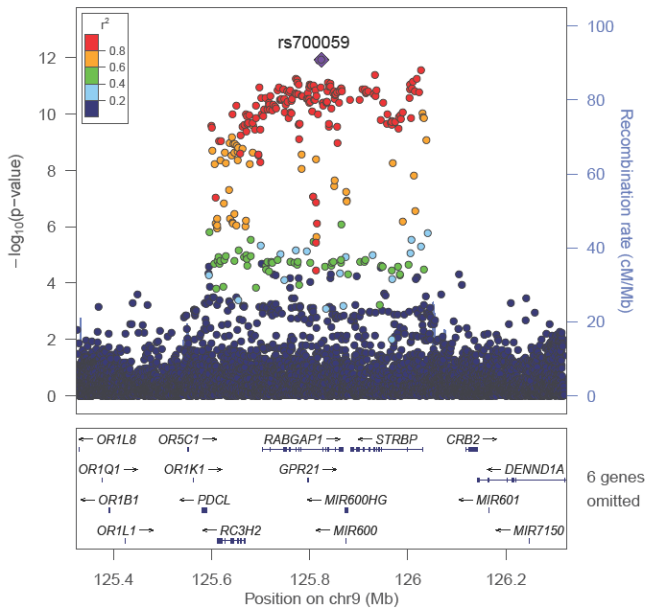

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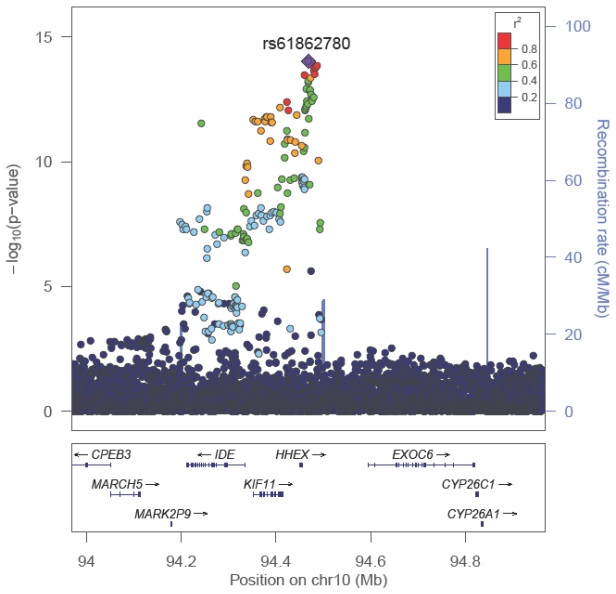

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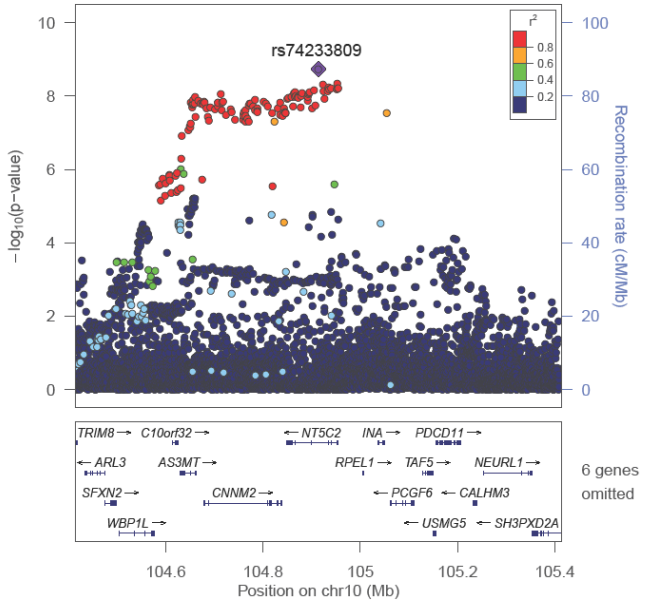

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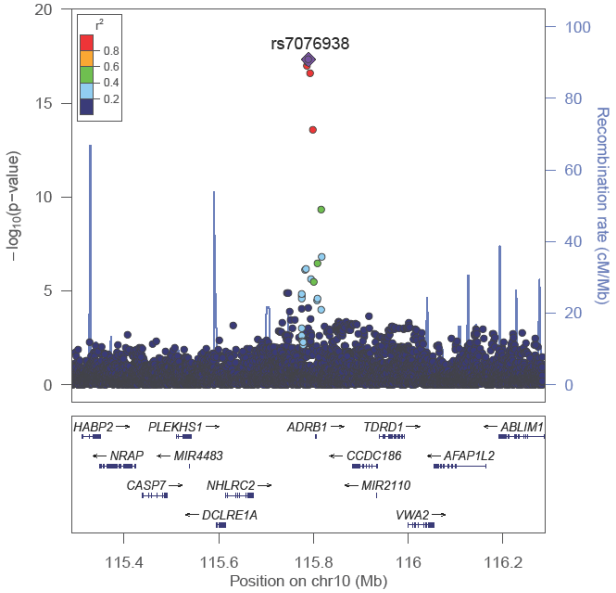

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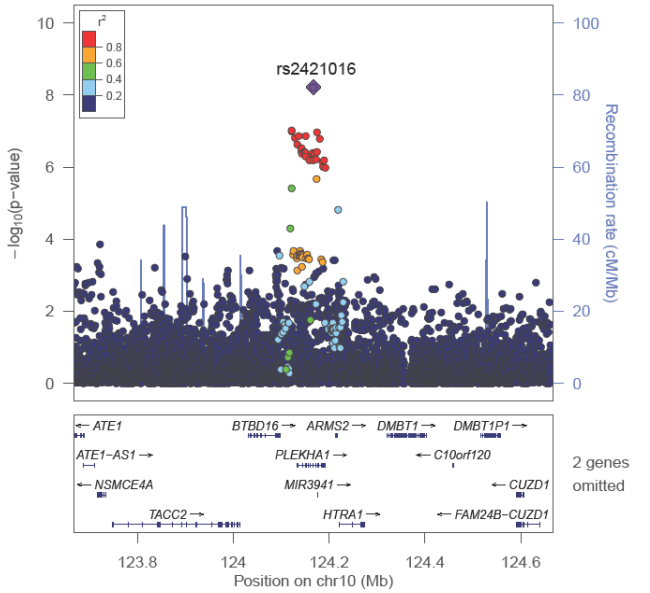

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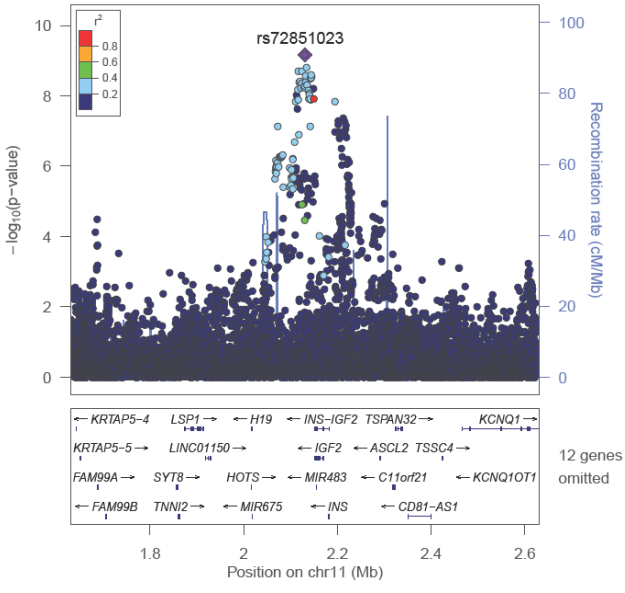

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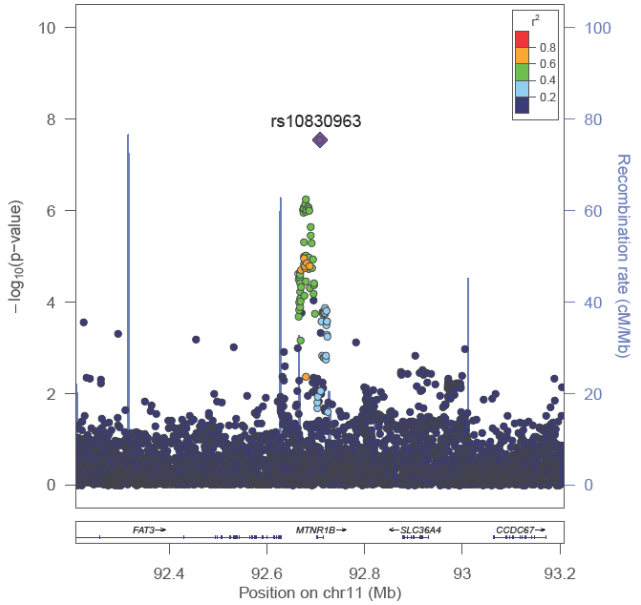

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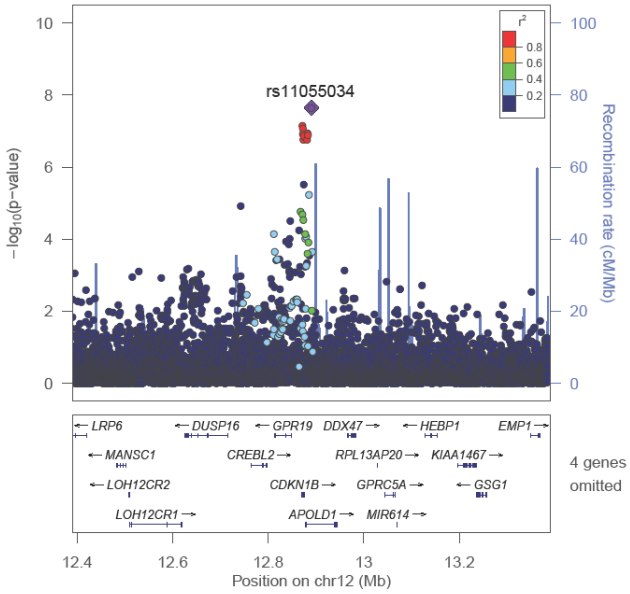

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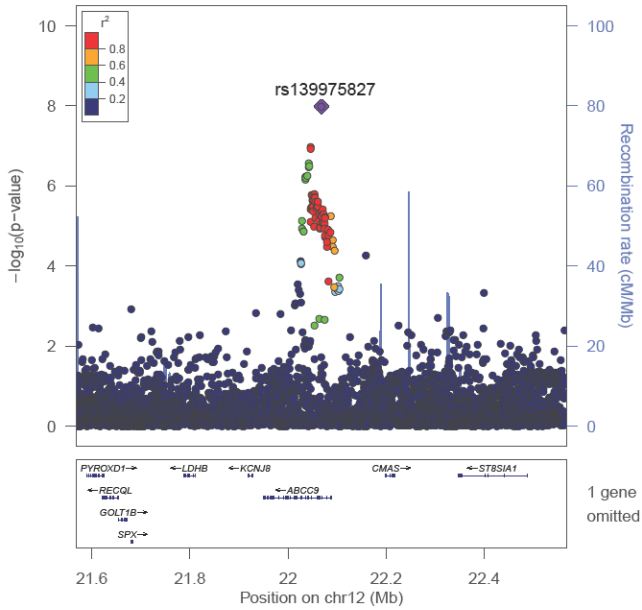

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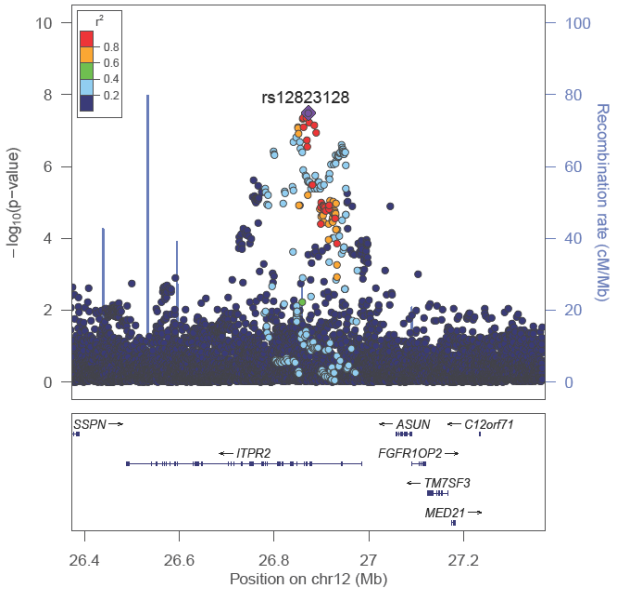

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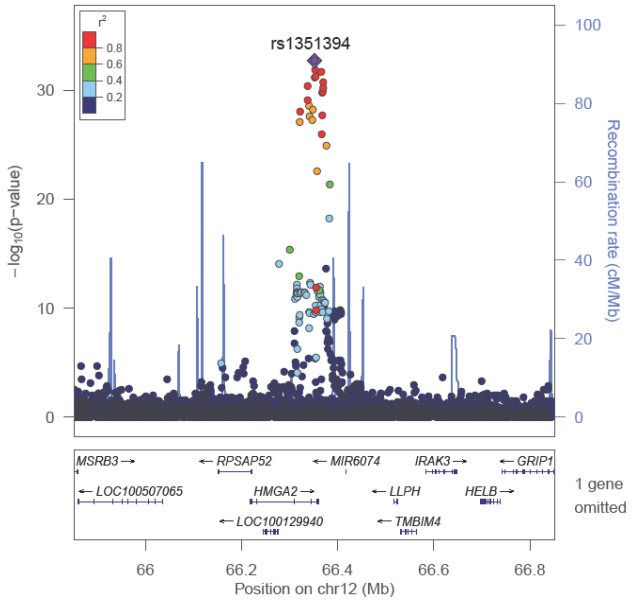

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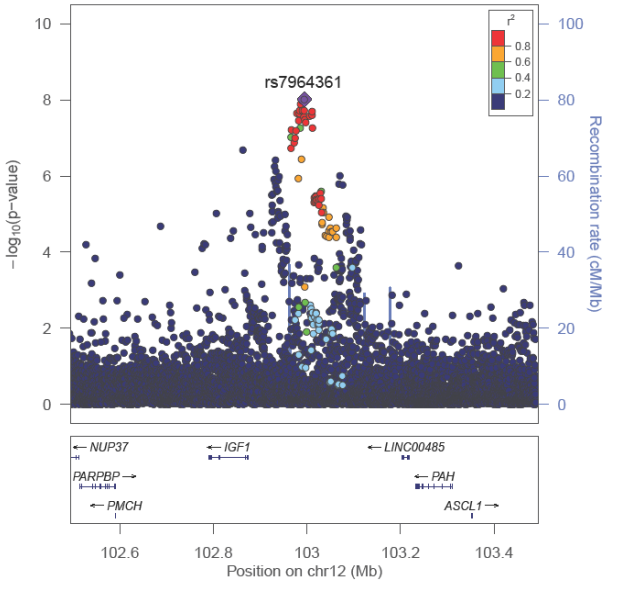

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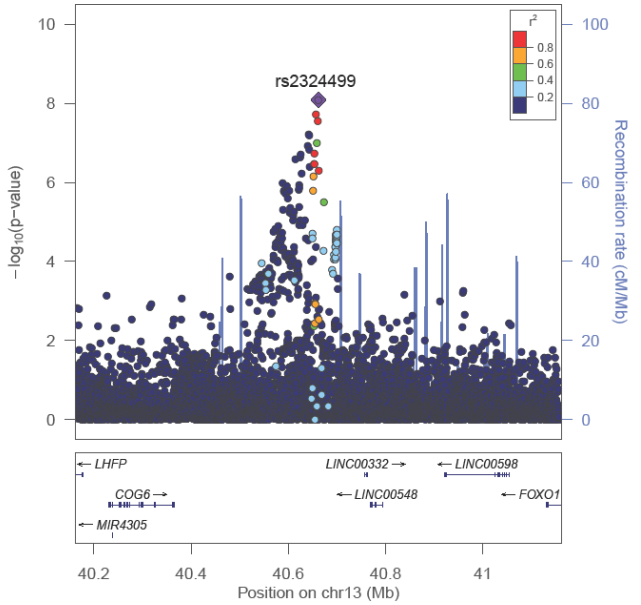

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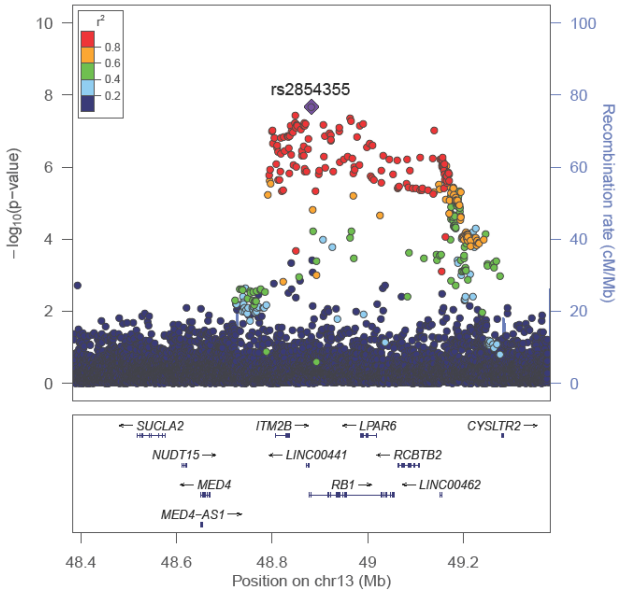

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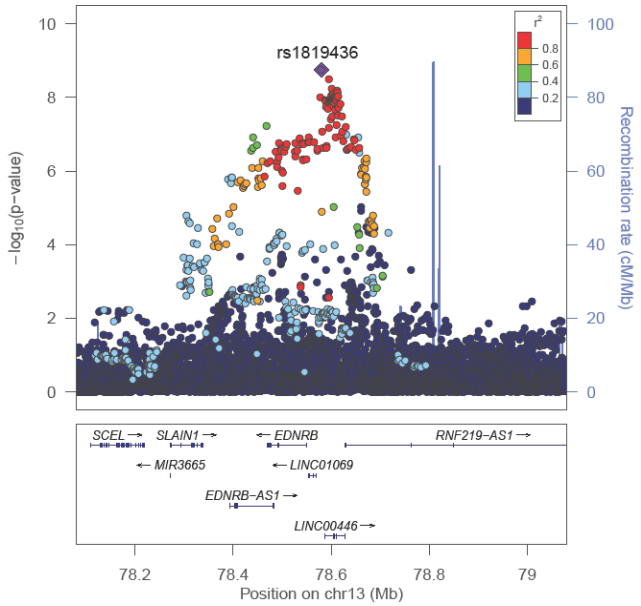

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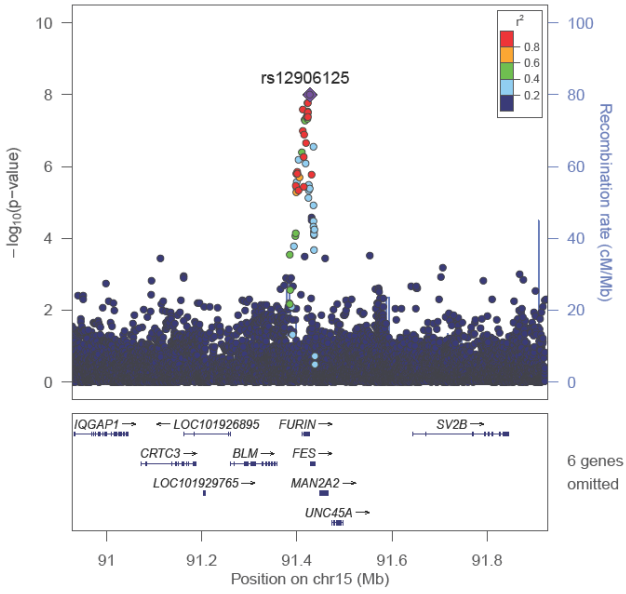

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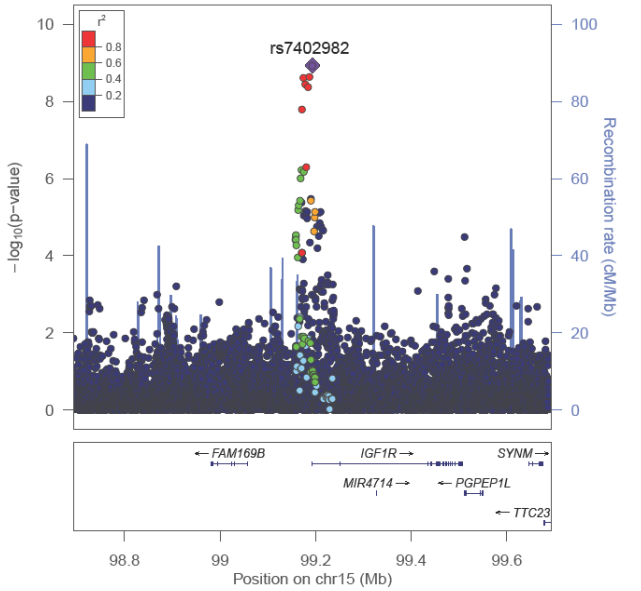

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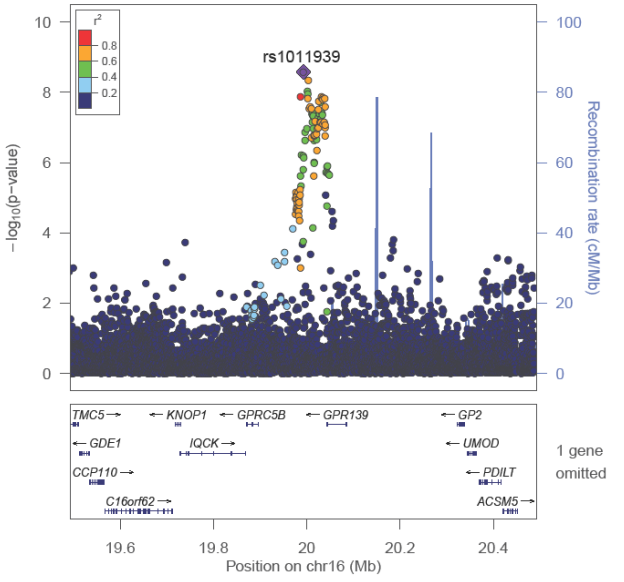

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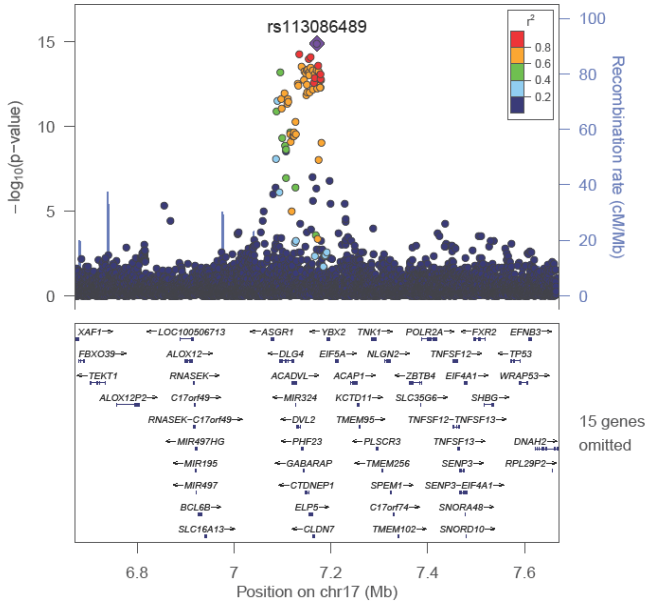

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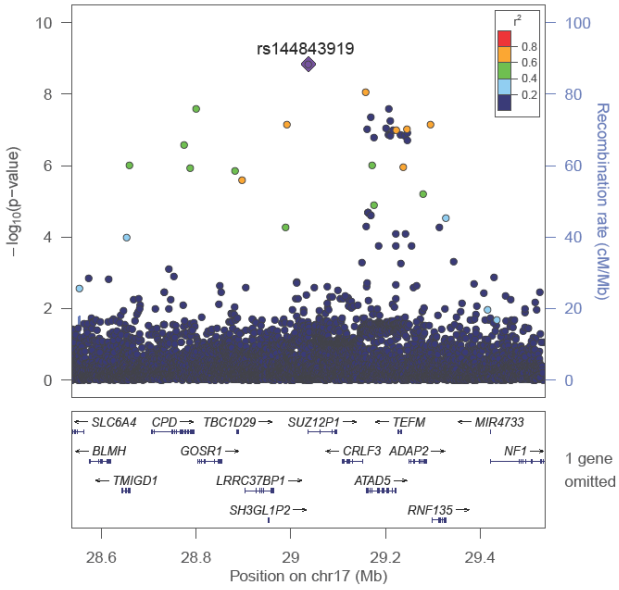

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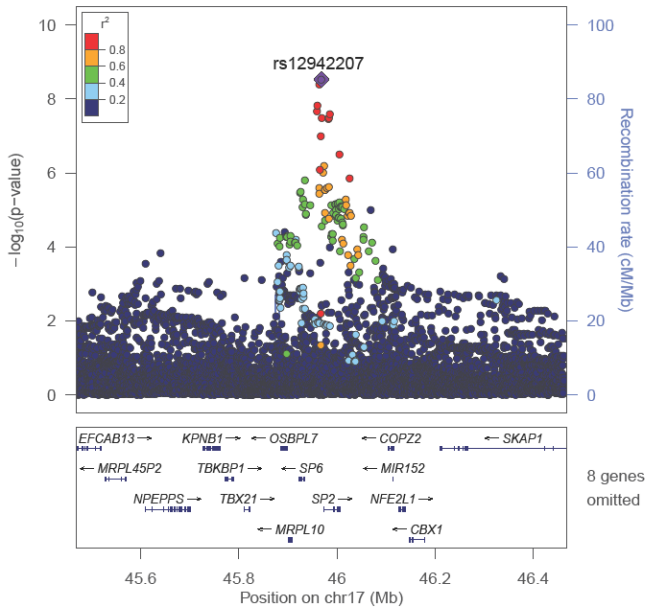

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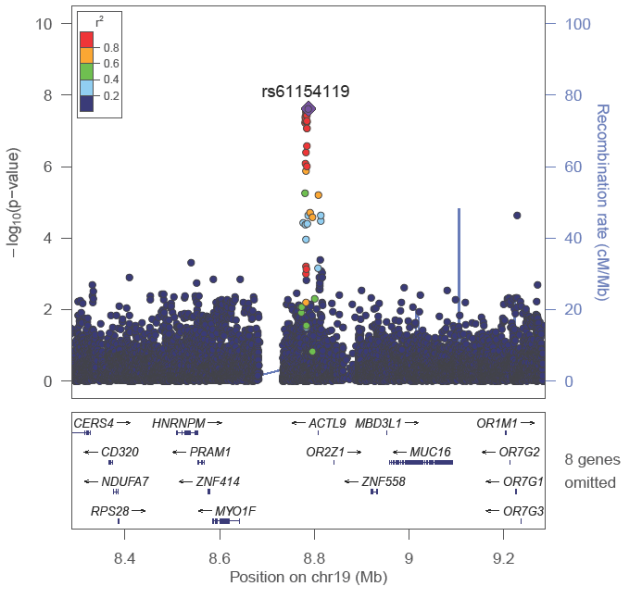

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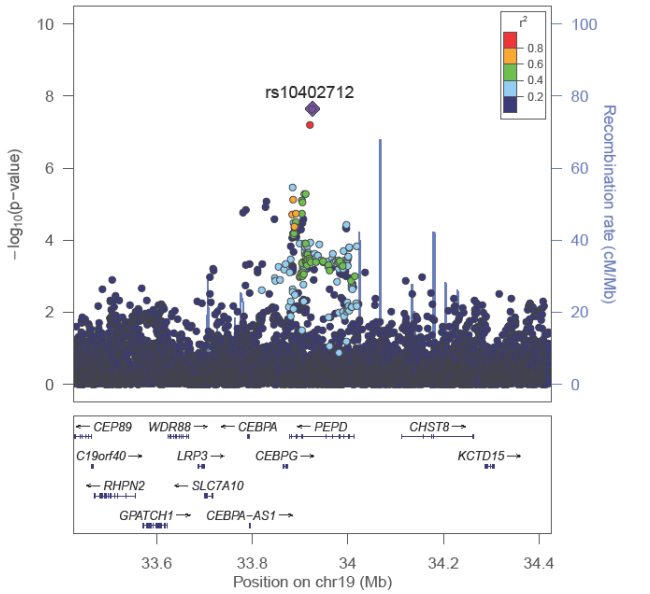

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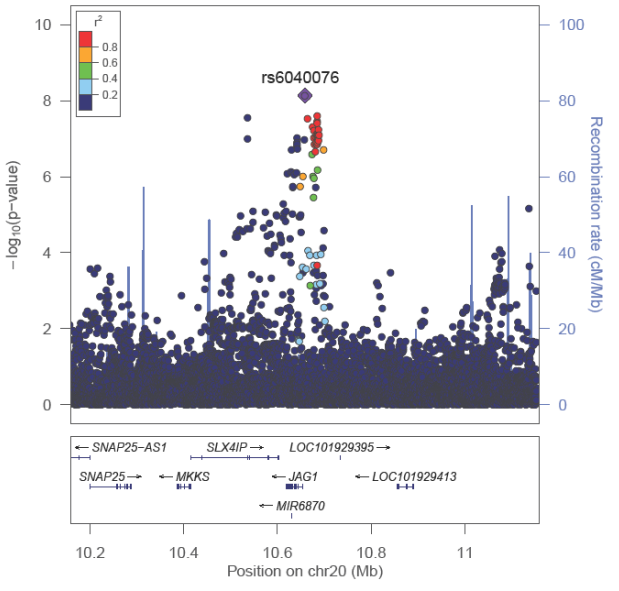

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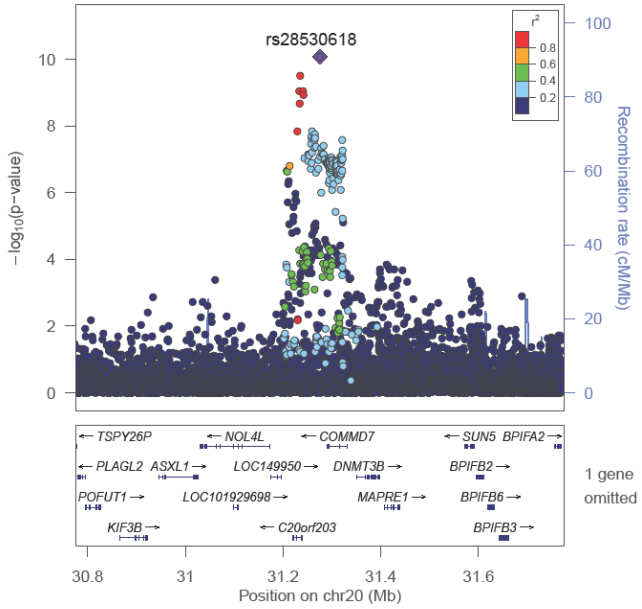

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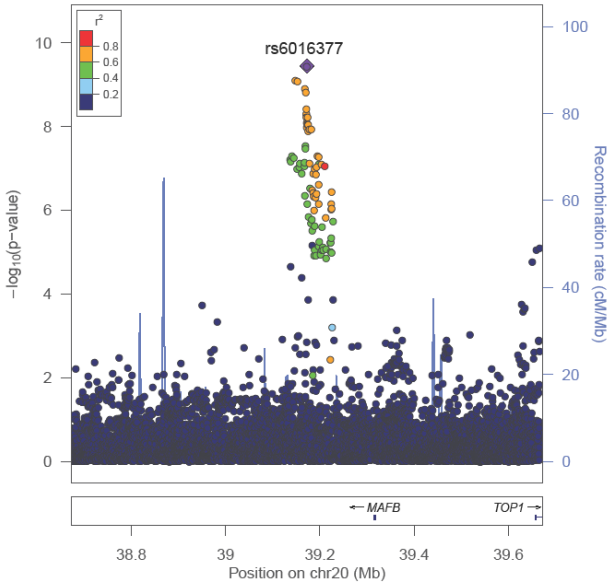

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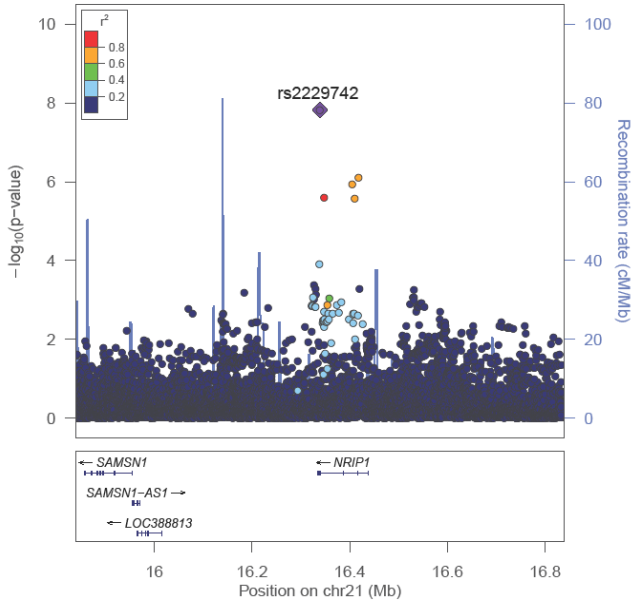

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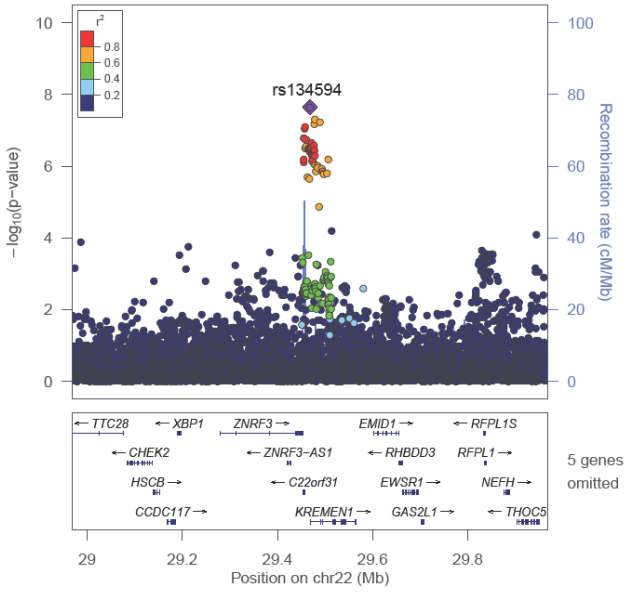

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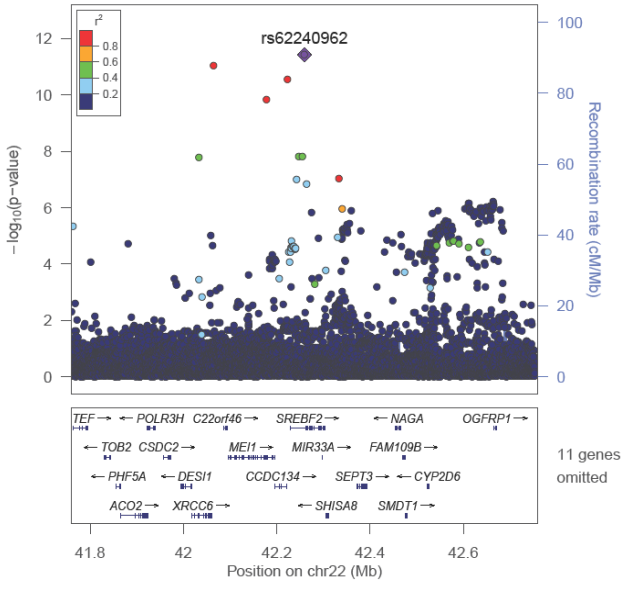

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